NAVMED P-5088

UNITED STATES NAVY Medical News Letter

Vol. 47 Friday, 7 January 1966 No. 1

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United States Navy
MEDICAL NEWS LETTER

Vol. 47 Friday, 7 January 1966 No. 1

Policy

The U.S. Navy Medical News Letter is basically an official Medical Department publication inviting the attention of officers of the Medical Department of the Regular Navy and Naval Reserve to timely up-to-date items of official and professional interest relative to medicine, dentistry, and allied sciences. The amount of information used is only that necessary to inform adequately officers of the Medical Department of the existence and source of such information. The items used are neither intended to be, nor are they, susceptible to use by any officer as a substitute for any item or article, in its original form. All readers of the News Letter are urged to obtain the original of those items of particular interest to the individual.

Change of Address

Please forward changes of address for the News Letter to Editor: Bureau of Medicine and Surgery, Navy Department, Washington, D.C. 20390 (Code 18), giving full name, rank, corps, and old and new addresses.

FRONT COVER: U.S. NAVAL HOSPITAL, JACKSONVILLE, FLORIDA. The final drawings for this hospital replacement project are completed and are out for bids. Bid opening is scheduled for 16 December 1965.

The new hospital structure will be an 8-story building. There will be no basement because of site and ground conditions. The design concept centers around a large block at ground level containing clinics and ancillary services with a tower unit rising above to complete the eight floors. The roof area contains penthouses and part of mechanical area. The ground floor contains the outpatient clinics, including Dependents' Walk-In Treatment Clinic; Medical Clinic; Surgical Clinic; OB/GYN Clinic; Emergency Room; Military Sick Call; EENT; Orthopedic Clinic; Laboratory; Pharmacy; Radiology; administrative functions, such as Commanding Officer; Executive Officer; personnel offices; food service facilities, both dining rooms and galley; central sterile supply, bag storage, and mechanical equipment.

The basic concept for the nursing unit consists of bedrooms on the perimeter area of the nursing unit tower. The ancillary facilities, such as Nurses' Station, utility rooms, baths, offices, examining rooms, and diet pantries are contained in a central core. All patient spaces are contained in bedroom accommodations; there are no large open ward-type spaces as in earlier designs of naval hospitals.

The hospital contains a gross area of approximately 233,300 SF and will be located on the site of the old hospital. The siting of the new hospital is such that the existing temporary hospital will be able to continue operation during the construction period of the new hospital.

Initial work on the site preparation is currently under way. It is hoped that the work on the main structure will begin in the first part of the new year 1966.

The issuance of this publication approved by the Secretary of the Navy on 4 May 1964.

FEATURE ARTICLE

NON-PENETRATING ABDOMINAL TRAUMA

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The startling appearance of penetrating injuries of the abdomen makes the necessity for operative intervention obvious. The question is not whether, but rather when surgery is best undertaken. On the other hand, closed or non-penetrating trauma produces a clinical dilemma, and as a result is often mismanaged. Mortality in large series of non-penetrating trauma may be as high as twenty to thirty percent.[1] Such a forbidding mortality rate is due in part to accompanying cranial or cardiopulmonary trauma, but delay in the diagnosis of serious intra-abdominal injury is a significant factor. The physician unaccustomed to the management of trauma inevitably overlooks major non-penetrating intra-peritoneal injuries because his attention is drawn to the more obvious head, chest, or extremity wound.

It is the purpose of this review to summarize some of the recent advances in the treatment of closed abdominal trauma which help both in recognizing major injury and its proper surgical management.

Emergency Care

As with any major injury, the principles of maintenance of airway, fluid replacement to overcome oligemia; induction and monitoring of urine secretion; establishment of naso-gastric suction; and proper care of wounds with high priority must be achieved first. The single most valuable device in the management of patients with non-penetrating abdominal trauma is available to every physician without cost or necessity for requisition—it is a high index of suspicion.

Any patient who has suffered trauma to multiple areas and remains hypotensive despite seemingly adequate local wound care and fluid replacement should be presumed to have major life-threatening intra-abdominal trauma until proven otherwise. Even the most lethal type of cerebral injury does not cause hypotension or shock. Other more obvious forms of trauma such as compound fractures, laceration of the face, and head or chest injuries must not divert attention from the abdomen.

Diagnosis

The decision for or against laparotomy in patients with blunt abdominal trauma represents a clinical challenge. The answer—ready made in penetrating wounds—must be made as early as possible to reduce subsequent mortality. Awaiting advanced signs of peritoneal irritation may be fatal. Fortunately, several new techniques are now available in making this difficult decision.

Abdominal paracentesis is a useful diagnostic procedure. In patients with non-penetrating abdominal trauma, it is standard practice to perform the so-called four-quadrant peritoneal tap. A IV 18 gauge needle or small polyethylene catheter is inserted into the peritoneal cavity at the four abdominal quadrants, aspiration carried out, and the returns examined for any abnormal material. Puncture of the bowel with the needle rarely occurs and is of no serious consequence. A positive tap is an indication for exploration; negative results are, of course, not conclusive.

Recently a method of peritoneal lavage has been described which improves the results of peritoneal aspiration and can be done safely and quickly.[2] The technique is: (1) In the midline, 6–10 cm below the umbilicus a small incision is made in the skin; (2) A plastic catheter (#14 French) with multiple small holes in the end is inserted into the peritoneal cavity through the incision; (3) One or two liters of physiologic saline is introduced intraperitoneally: (4) The patient is turned from one side to the other for thirty seconds three to four times; (5) The fluid is aspirated. The presence of hemoglobin, amylase, bacteria (on smear), or vegetable fibers suggests

either intraperitoneal hemorrhage, solid organ injury, or hollow viscus perforation and means exploration is necessary. The authors report 100% accuracy in more than 100 cases as compared to the 67 to 86% for classical peritoneal tap.

X-ray examination may be helpful if the severity of intraperitoneal injury is in doubt. The development of lightweight litters with means of firmly strapping the patient in place (Ferno-Washington Company, Greenfield, Ohio) and air pressure splints (Kendall Company, Bauer-Black Division, Chicago, Illinois) permits safer manipulation and more thorough x-ray examination of the injured. A lateral decubitus x-ray examination with the patient and litter turned on the side or a cross-table lateral examination may be as satisfactory as an upright film in showing free peritoneal air.

Intravenous pyelograms or cystograms are both safe and often essential in evaluating patients with hematuria, pelvic fractures, and suspected bladder rupture. Often they are the only means of accurately localizing the urinary tract injury.

Operative Management

Liver injury in blunt abdominal trauma still carries an extremely high mortality rate (45%) because of uncontrolled immediate hemorrhage, delayed bleeding, or eventual peritonitis due to leakage of bile.[3,4] The basic principles of handling the injured liver are: arrest of hemorrhage, removal of devitalized tissue, and provision of external drainage to prevent bile peritonitis. Hemostatic packing should be avoided because of subsequent tissue necrosis and infection. Adequate drainage is best provided by a sump-type drain. The occasional need for lobectomy or partial hepatectomy necessitates familiarity with the technique.[4] Anatomically, the liver is divided into a right and left lobe by a line in the plane of the gallbladder and inferior vena cava, not at the area of the falciform ligament. Lobectomy is achieved by isolation and ligation of the portal vein and hepatic artery branches going to the lobe involved prior to incising the liver. Large overlapping mattress sutures should be placed into the liver substance and tied down at the proposed line of cleavage for further hemostasis.

Drainage of the common bile duct with a T-tube following liver injury is currently under evaluation. It is performed in order to decompress the biliary tract and to prevent leakage of bile and pancreatic juice from the lacerated liver. Injection of saline into the common duct via the T-tube at the time of emergency partial hepatectomy can be used to disclose lacerated biliary radicals which require individual ligation. Although the successful use of T-tube drainage has been reported in 10 recent cases of liver injury,[3,4,5] its routine use requires additional clinical trial.

The duodenum, because of its anatomic fixation, may be lacerated at the time of non-penetrating injury. A large, gaping hole in the side of the duodenum may defy ordinary methods of closure and subsequently result in either a fistula or an obstruction. Successful primary closure of such defects can be achieved by using a loop of jejunum as a "patch" over the torn duodenum. The serosa of the jejunum is sutured circumferentially around the opening in the wall of the duodenum, placing the sutures far enough away from the tear so that good serosa-to-serosa approximation can be made. Thus, the serosa of the jejunum is exposed to the internal contents of the duodenum. Experimentally, duodenal mucosa closed the gap in about 8 weeks.[6] If a fistula develops, it will occur internally into the jejunum causing no harm. External drainage of the traumatized retroperitoneal area is mandatory.

When duodenal injury or retroperitoneal hemorrhage is encountered during an exploration for suspected intraperitoneal injury, the pancreas must be thoroughly inspected. Obviously hemorrhage, which invariably accompanies any trauma to the pancreas to the left of the superior mesenteric vessels is best treated by distal pancreatic excision, precise ligation of the main pancreatic duct, and sump drainage of the retroperitoneal space. Complete or partial transection of the pancreas to the right of the superior mesenteric vessels is best treated by suture of the duct over a splint placed transduodenally through the ampulla or internal drainage of the distal pancreas into a Roux-en-Y loop of jejunum. The proximal duct is tied off and the pancreatic area provided with sump drainage. Contusion of the pancreas, no matter how severe, should be drained—preferably with a sump tube. If an external pancreatic fistula develops, it closes 90% of the time, although it may take as long as three months to do so.

Life-threatening hemorrhage from lacerated pelvic vessels may accompany severe lower abdominal trauma with almost no external evidence of the site of the bleeding. Indeed, unresponsive hypotension in the presence of pelvic fracture should be assumed to be due to such occult retroperitoneal bleeding and pelvic laparotomy undertaken. Ideally each source of bleeding should be identified and secured; the pelvic veins may retract and make this extremely difficult. Under these trying circumstances, the alterna-

tives are: (1) packing the pelvis—characteristically followed by infection and sometimes resulting in fatal septicemia; or (2) unilateral or bilateral internal iliac artery ligation. The latter procedure has been advocated by gynecologists in the control of uterine hemorrhage, and has been recently reported as a successful means of controlling hemorrhage following pelvic trauma.[7] Sump drainage to the outside will avoid further hematoma formation and infection.

Complications

Arterial hypertension occasionally follows blunt abdominal trauma to the kidney. The IVP at the time of the injury may show unilateral delayed or non-function or a mass which suggests hemorrhage and necessitates exploration. Nephrectomy is rarely necessary under these circumstances. Follow-up IVP examinations must be done if hypertension persists. These may show unequal function and the presumed reason for the hypertension, namely excess renin released from poorly perfused renal tissue. Probably, less than 10% of such patients will develop such postinfarction renal hypertension, but under such conditions nephrectomy is curative of the hypertension.

Hemobilia is a term which was coined in 1948 by Sandblom [8] to describe abnormal bleeding through the biliary tract into the gastrointestinal tract. The lassic symptoms following hepatic trauma are biliary colic and gastrointestinal bleeding manifested by hematemesis or melena.[9] Their occurrence may be avoided by individual ligation of lacerated biliary radicals and careful intrahepatic hemostasis at the time of emergency laparotomy. Cholangiography may be helpful in localizing the site of hemorrhage within the biliary tract. This is an additional reason for putting a T-tube into the common duct at the time of the original exploration.

Pancreatic pseudocysts are common following blunt trauma to the pancreas. The diagnosis is always suspect when a patient who has had blunt abdominal trauma develops an enlarging epigastric mass or abdominal tenderness, and fever. They occur in the absence of emergency surgery at a greater rate than when pancreatic exploration and drainage are performed. The type of pancreatic drainage used is also important. In one study [10] the complication rate was as follows: in 66.6% with no drainage; 21.9% with Penrose drainage, and 10% with sump drainage, corresponding pseudocyst formation rates were 66.6%, 28.5% and 0%. Pseudocysts (or continuing external pancreatic fistulae) are best treated by internal drainage into a Roux-en-Y loop of jejunum.

Emergency angiography. Lacerations and thrombosis of major vessels may occur with blunt abdominal trauma. Emergency angiography is helpful in localizing the site of major arterial damage. Once normal blood pressure has been restored in an injured patient, absence of femoral pulsation, femoral artery bruit, or increasing abdominal girth, in the presence of negative peritoneal lavage, are indicative of injury to major retroperitoneal vessels. Rarely, emergency angiography via a translumbar needle or brachial artery catheter will be helpful in localizing the lesion and in permitting a more intelligent surgical approach. Late sequelae of abdominal aortic rupture are the development of a false aneurysm or very rarely an aorto-caval fistula. Both are amenable to surgical repair.

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EDITORS NOTE: Three recent reports of Blunt Injury to the Abdomen supplement the Feature Article, in this issue of the News Letter, on this subject by Dr. Griffen. All are in the November issue of *Annals of Surgery*.

THE USES OF GAMMA GLOBULIN IN PROPHYLAXIS AND TREATMENT

Robert J. Roantree MD. The Medical Clinics of North America, Basic and Clinical Immunology 49(6): 1745-1756, November 1965.*

In this paper, I shall present a background based on several excellent review articles, and a more detailed account concerning recent reports on the clinical use of gamma globulin.

The introduction of the Cohn techniques for the fractionation of plasma in the 1940's made possible the production of human gamma globulin on a scale sufficient to allow its use for passive immunization against many of the common infectious diseases. Plasmapheresis has provided a means for collecting large amounts of plasma from convalescent or actively immunized donors. Thus, preparation of human immune gamma globulin is possible for those infections against which there is insufficient antibody in pools of normal sera.

These preparations from human plasma afford a number of advantages over the agents used for passive immunization in the past. As will be documented below, they incite many fewer allergic reactions, give longer and more certain protection, and since they can be used in lower dosage, interfere less with the response to active immunization than do heterologous antisera when simultaneous passive-active immunization is desirable.

Reports of serious allergic reactions have been scant indeed. A review of the few alleged anaphylactic reactions up to 1961 cast doubt that any were truly anaphylactic reactions to the gamma globulin itself. It is now known that patients receiving multiple injections may develop antibodies against the Gm factors absent in their own sera, and thus a mechanism for allergic reactions exists. But experience to date indicates that such occurrences will be rare. There are occasional local inflammatory reactions with associated mild fever and malaise. A figure of 1.2 per cent has been reported for their occurrence. Intravenous administration would, of course, be very advantageous in those patients receiving large doses, but such injections are followed by febrile reactions in a high percentage of cases.

Fractionation of the plasma not only accomplishes the concentration of the gamma globulin into a volume generally suitable for intramuscular injection but also eliminates the virus of serum hepatitis. Antibodies in the gamma globulin preparations are remarkably stable and retain their effectiveness for many years. It is distributed as 16.5 per cent solution usually with 1:10,000 merthiolate as a preservative. It is administered subcutaneously or intramuscularly and, if large volumes are required, the dose may be divided and injected into different sites.

Tetanus

I shall consider the use of hyperimmune human gamma globulin in tetanus first since it demonstrates most conclusively the advantages of using the homologous human product as opposed to heterologous horse antiserum in passive immunization, and particularly in active-passive immunization.

The use of plasmapheresis has allowed the harvesting of plasma from recently immunized donors in sufficient quantity so that hyperimmune antitetanus gamma globulin is commercially available. Evidence has accumulated that, aside from its freedom from producing hypersensitivity reactions, this product is more effective than horse antiserum, and since it can be used in a smaller dose it is less likely to interfere with the active antibody response to tetanus toxoid.

Every practitioner treating tetanus must have had qualms about using horse antiserum. In trying to assess the morbidity caused by serum sickness in Canada, Toogood estimated that 7900 severe allergic reactions to horse antitetanus serum occurred annually in that country. He concluded that the morbidity (but not the mortality) from these allergic reactions approximated, and at times, exceeded that from tetanus itself. It has been estimated that there is a risk of about 1 in 100,000 having fatal anaphylactic reactions and 20 to 30 per cent delayed reactions. Others have concluded that the risk of delayed reactions is as low as 5 per cent.

Several investigators have shown that horse antitetanus antibodies disappear more rapidly than hu-

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man antibodies from the human circulation. The half-life of the latter has been calculated as four weeks as compared with between one and two weeks for the horse antibodies. The rapid removal of heterologous antibodies after the seventh postinjection day due to the recipient's antibody response to the foreign globulin has been confined in guinea pigs. These authors also found that guinea pig antitoxin was at least 100 times as effective in protecting the guinea pig against challenge with the toxin as was a heterologous antitoxin. They list the advantages of using a homologous antiserum as: (1) less likelihood of immune reactions, (2) predictable levels of antitoxin can be achieved as compared with a great variability of disappearance of horse antiserum, (3) protective and persistently high levels of antibody are attained following a much lower dose. These studies and those of McComb are in agreement that an effective adult dose of human immune antitetanous toxin should be about 250 units. Rubenstein makes a special plea for using a dose based on body weight of from 3 to 9 units per kg. This compares with the 5 units per kg. recommended by Rubbo and Suri.

When horse antiserum was given simultaneously with tetanus toxoid, 1,500 units possibly interfered with one of four active responses in the human, but 500 units did not in 23 instances. Theoretically, the smaller dose of human antitoxin should show less interference. That 250 units given in a separate site simultaneously with the toxoid does not interfere has been demonstrated.

The evidence, then, is in agreement that human immune globulin is a much safer and effective agent than horse antiserum. Nevertheless, it seems unfortunate that passive immunization should be necessary when adequate active immunization is a much better means for protecting the population as a whole. This is particularly true since it is estimated that over half of the cases of tetanus occur following injuries thought too trivial to report to a physician so that there is no opportunity for early passive immunization. What may happen in times of disaster has been illustrated by the occurrence of 40 cases per 1,000 wounded civilians in the battle of Manila in World War II, and such figures have been used to mount the recent campaign for active immunization. Since an appreciable proportion of cases of tetanus is neonatal, perhaps one way of preventing this while immunizing part of the female population in which immunity has lapsed would be to advocate a booster during the last month of pregnancy. Complete courses of active immunization of a group of mothers have been carried out in Thailand where tetanus is responsible for 28 per cent of neonatal deaths.

Gamma globulin is used to treat tetanus after the development of symptoms, but its effectiveness is difficult to evaluate.

Diphtheria

Although immunization procedures for diphtheria are similar to those for tetanus, the problem of whether to immunize passively has not been as great. Little information is available on the use of normal human gamma globulin; commercial hyperimmune gamma globulin is not available.

Measles

The effectiveness of gamma globulin obtained from normal human donors to attentuate or prevent measles in susceptible exposed children is well documented. A dose of 0.1 ml. per lb. body weight given within six days after exposure prevents the disease in 80 per cent of intimately exposed contacts, and 0.02 ml. per pound usually attenuates the disease if given during the same time period.

Since the introduction of the live measles vaccine, a major use of gamma globulin has been in the prevention of the milder, but bothersome, signs and symptoms caused by the vaccine itself. The evidence is convincing that the injection of gamma globulin simultaneously with the live vaccine but into a different site greatly reduces or eliminates the undesirable effects of the vaccination without interferring with the early antibody response to the vaccine. There are data indicating that, after two years, antibody titers are somewhat lower in a group of children receiving the gamma globulin than in those receiving only the vaccine, but both groups show complete immunity to challenge after that period. The usual dosage of gamma globulin given for this purpose is 0.01 ml. per lb. body weight.

A promising approach to the amelioration of the disease caused by the live vaccine is pre-immunization with one to three injections of 0.5 to 1 ml. doses of killed measles vaccine, and then injection after a variable length of time (usually about six months) of 0.5 ml. of the live virus preparation. This procedure in the few trials reported seems slightly superior to the use of gamma globulin and live vaccine, both in reducing the incidence of signs and symptoms from the vaccine and in lack of inhibition of the antibody response. It is particularly encouraging that this scheme seems perfectly adaptable to the present scheme of infant immunization. If the

killed vaccine is given along with the DPT injections, the live vaccine can be given six months to a year later.

Another approach that may eliminate the need for gamma globulin for the prevention of measles is the use of a further attenuated virus vaccine. Both of these latter approaches require long-term evaluation, but they may prove a less expensive alternative to gamma globulin and a means of preserving the supply of this for the prevention of such diseases as infectious hepatitis, against which we possess no effective procedures for active immunization.

Infectious Hepatitis

Gamma globulin prepared from pools of plasma from normal donors has been the most effective in the prevention of measles and of the clinical jaundice of infectious hepatitis, probably because the donors have nearly all had measles and many have had inapparent infectious hepatitis. Evidence is strong that the effect of the gamma globulin, whether given in the usual dosage of 0.01 ml. per lb. body weight or in doses as high as 0.06 ml. per lb. body weight, is to ameliorate infectious hepatitis rather than prevent infection. Thus, the protected infected subject still gains the advantage of an actively induced immunity.

Most of the data upon which the above statements are based have come from institutional situations in which much of the population was continually at risk. The use of gamma globulin to prevent epidemics in a general population has been studied more extensively recently. In an urban outbreak in Iowa, 90 per cent of all family contacts received 0.01 ml. per lb. body weight as soon after contact as possible; five of 1,577 developed clinical jaundice, while 14 of 133 contacts not receiving gamma globulin developed it. Convincing data are presented that its use effectively suppressed clinical disease in a closed community in Alaska, and prevented jaundice in a school epidemic in England. A dose of 0.005 ml. per lb. may be as effective as 0.01.

A special problem of modern times is the visitor to foreign areas where the disease is endemic. If the stay is a prolonged one, 0.06 ml. per lb. should afford protection for about six months.

Serum Hepatitis

The report that serum hepatitis occurred in 3.9 per cent of patients over 40 years old receiving transfusions, and that 23 per cent of these died, focused attention upon the possible use of gamma globulin as a preventive measure. Mirick and coworkers reported a series of over 1,000 transfused patients, of whom about half were treated with 10 ml. of gamma globulin one week after transfusion and another 10 ml. one month later. Four per cent of the untreated patients developed jaundice as compared to 1.1 per cent of the treated group. Although such use of gamma globulin in all patients over 40 receiving multiple transfusions was suggested editorially, it has been pointed out that this would take much more gamma globulin than the recent rate of production could supply.

If the present concept that the viruses of infectious hepatitis and serum hepatitis are separate entities not conferring cross-immunity is correct, it seems unlikely that gamma globulin from a pool of normal donors would contain enough antibody against the serum hepatitis virus, since the incidence of this disease is much less than that of infectious hepatitis (unless there is considerable undiscovered infection). Perhaps the suggestion that some of the infections Mirick's group were studying were actually infectious hepatitis is the correct one.

In a recently reported study, three of five subjects challenged with 5 ml. of plasma from a pool known to cause jaundice developed the disease. Twenty subjects were challenged in the same manner and given in addition eight 250 ml. infusions of plasma from a pool of aged convalescent serum over a five-month period. None developed jaundice. At this time more information is necessary to judge whether gamma globulin is of use in this disease.

Rubella

The general problems of control of the two types of hepatitis and of rubella are similar. Ultimate solutions to each will require the isolation and dependable cultivation *in vitro* of the casual agents. There have been a number of reports of the isolation of the agents of hepatitis, but the reproducibility of these results from laboratory to laboratory has been most difficult. At the present time, it looks as if the artificial cultivation of rubella is further advanced, and its isolation from active human cases feasible. This progress gives hope that a live active immunizing agent will become available in the next few years. In a disease as mild as rubella in the young, perhaps attenuation of the virus is unnecessary, and vaccination of the female population prior to the child-bearing period may eliminate the problem of congenital defects occurring in infants whose mothers contract rubella in the first trimester of pregnancy.

A recent report on a long-time follow-up of a large British prospective study indicates that 15 per cent of the children whose mothers had rubella during the first 16 weeks of pregnancy had major congenital defects involving usually the eyes, ears or heart. Such results are in accord with many other studies and leave no doubt that the problem is serious. Now that the virus can be cultured, the entity of newborn rubella is being recognized. It is characterized by retardation of growth, generalized purpura, hepatosplenomegaly, encephalomyelitis and lesions of the long bones, and it often leads to early death. Virus can be cultured despite high titers of antibody in the cord blood.

There have been confusing results from attempts to assess the value of gamma globulin in preventing rubella, and especially its ability to prevent malformations of the newborn. The latter is the more difficult problem because it is not clear that suppression of symptoms and signs in the mother is sufficient to protect the fetus unless viremia is completely suppressed also. The question of whether a pregnant woman has been exposed is complicated by the fact that the virus has been detected in the nasopharynx of a child as long as 13 days prior to the rash and as many as 40 per cent of children with infection showed no rash.

Data from a recent epidemic clearly indicate that gamma globulin with an antirubella titer of 512 given in a dose of 0.25 ml. per lb. body weight protected against the clinical disease. Eighteen per cent of 49 boys so treated developed the disease compared to 89 per cent of 56 untreated girls. Fifteen of the boys had an antibody rise despite absence of symptoms, indicating subclinical infections. The titer of this lot may be considered as average or low for commercial gamma globulins, since a survey done on 19 different lots showed them to vary from 256 to 1,048, and these compared to a titer of 2,096 obtained from a lot of gamma globulin prepared from convalescent serum.

The more difficult problem of whether gamma globulin protects against fetal damage is not easily answered. Most surveys have seemed to show a lower incidence of rubella and consequent fetal damage in exposed women treated in the first trimester of pregnancy, but some have shown no effect. The usual explanation for this variation in results has been that there are differences in the antirubella titers of the lots of gamma globulin used. On the basis that most reported series show a lowered incidence of fetal anomalies after gamma globulin, it seems best to give 20 ml. of gamma globulin to any nonimmune woman exposed to rubella during her first trimester, with the realization that this may not be effective in the prevention of viremia and consequent fetal deformities.

Mumps

The problem of the use of gamma globulin in the prevention or alleviation of mumps resembles that of rubella because it seems worthwhile in only a segment of the population, in this instance, the nonimmune adult male. The data from one study are convincing. Four of 51 recruits given 20 ml. of hyperimmune gamma globulin within 24 hours after developing mumps parotitis subsequently suffered orchitis as compared to 14 of 51 controls. There seem to be no data to indicate whether smaller doses might be effective, although 2.5 and 5 ml. doses have been recommended. In the above study 50 ml. of normal gamma globulin were ineffective. If the treatment seems indicated, only hyperimmune gamma globulin should be used. It is commercially available.

Vaccinia and Variola

The complications associated with vaccination are of more importance in this country than smallpox itself. Evidence is convincing that immune gamma globulin reduces mortality in eczema vaccinatum and the morbidity in generalized vaccinia and accidental autoinoculation with vaccinia virus. The mortality from progressive vaccinia, nearly 100 per cent prior to the use of gamma globulin, was about 30 per cent with its use. Results from studies in which both immune gamma globulin and the recently introduced antivaccinal agent, N-methylisatin β-thiosemicarbazone, were used in this disease are encouraging. In one instance the latter agent seemed the more effective. It is to be stressed that this disease usually occurs in patients with immunologic defects, such as agammaglobulinemic children or adults suffering from lymphatic leukemia under treatment with corticosteroids or antimetabolites. Vaccination should be undertaken in such patients only if the indications are very strong and then it should be accompanied by gamma globulin.

A prophylactic indication for the use of gamma globulin is inadvertent vaccination of a child with eczema, or his exposure to a vaccinated sibling. A vaccinated patient coming down with varicella or receiving an extensive burn shortly after vaccination would fall into the same category. A dose of 0.6 to 1.2 ml. per kg. has been recommended.

Postvaccinal encephalitis is not often encountered here. A study in Holland on vaccinated recruits indicates that 2 ml. of gamma globulin given simultaneously with vaccination significantly reduced the incidence of this complication. Its use seems without effect after symptoms have developed.

A study in India of the use of gamma globulin to prevent smallpox in contacts of newly discovered cases revealed a 70 per cent reduction in those receiving it as compared to contacts not receiving it. The contacts were injected within 24 hours of case discovery, and children under five were given 5 ml. and adults 10 ml. of the globulin. A more recent study conducted along similar lines reveals a more dramatic decrease in morbidity and mortality using the antivaccinal agent N-methylisatin β-thiosemicarbazone.

Antivaccinal immune globulin can be obtained from the American National Red Cross if the indications for its use are sufficient.

Rabies

It is estimated that 32,000 individuals are given antirabies vaccine each year in this country. Most are now given duck embryo vaccine so that the risks inherent in the classical vaccine propagated in spinal cord tissue are lessened.

There is scant but convincing evidence that animal antisera are of great importance in protection against rabies. Seventeen victims suffering head and neck wounds from bites of a rabid wolf were studied. Five received active immunization alone with phenolized vaccine for 21 days. Three of these died and antibodies did not appear in their sera for at least 19 days. Twelve received either one or two injections of rabbit serum in addition to the active immunization. Eleven of these survived and antibodies were demonstrable in their sera early. An effort is now being made to collect a pool of human immune gamma globulin from those who have been vaccinated with the duck embyro vaccine because of exceptional.risk.This should provide a real step forward in the treatment of rabies.

Varicella

The indications for the use of gamma globulin to prevent or mitigate chickenpox are fewer and less pressing than in many of the other diseases. Such circumstances as the exposure of a nonimmune patient on corticosteroid therapy to varicella might make it desirable. One large study in which contacts received doses of from 0.1 to 0.6 ml. per lb. showed that there was no reduction in incidence of infection, but those receiving the gamma globulin had fewer pox and milder symptoms. For instance, the group receiving 0.1 to 0.2 ml. per lb. body weight had one-third as many pox as controls; those receiving 0.6 ml. per lb. had one-eighth the pox count of controls.

A dramatic reduction of pain in certain cases of herpes zoster has been observed after the administration of 10 ml. of normal gamma globulin. Large doses intravenously were used in another study with the same result.

Poliomyelitis

Since the introduction of the vaccines for active immunization, the question of prophylaxis has become a minor one. The bulk of the evidence from data collected prior to the immunization campaigns indicates that doses given prophylactically averaging 0.14 ml. per lb. were effective in reducing the incidence of paralytic poliomyelitis.

Bacterial Infections

The basis for the use of gamma globulin to treat infections dependent upon bacterial multiplication is not as well established as its use as an antiviral or antitoxic agent. It has been well shown that it helps keep hypogammaglobulinemic children free from the gram-positive coccal upper respiratory infections that usually afflict them. But the blood levels are maintained at concentrations much lower than those of the normal child, and it is not clear that gamma globulin treatment of a patient already possessing normal levels is beneficial in bacterial infections.

There is good evidence that gamma globulin is useful in preventing secondary infections following large burns. Under these circumstances, the loss of gamma globulin into blister fluid is very rapid, and 95 per cent of injected gamma globulin has been found to disappear in 48 hours in the case of a 60 per cent burn. In a large group of cases of burned children in Chile, it was found that either gamma globulin, 1 ml. per kg. on the first, third and fifth days, or large doses of plasma, reduced by 50 per cent the incidence of pseudomonas and staphylococcal septicemias. Administration of albumin and saline had no such effect.

The effectiveness of gamma globulin in the treatment of other types of bacterial infection is difficult to evaluate because other antimicrobial therapy is usually combined with its use. Studies have shown that human gamma globulin can protect mice against infection with a wide range of bacteria in-

cluding many of the gram-negative enteric bacteria, staphylococcus and streptococcus. Those with the greatest clinical experience believe its use has been definitely beneficial in certain cases including staphylococcal osteomyelitis and septicemias, and pseudomonas infections. In these instances large doses of gamma globulin were used—0.5 to 2.0 ml. per kg. or 10 ml. per day—often given intravenously in saline.

Most controlled studies have shown it to be of little use in the nonspecific prevention of infectious disease in populations prone to frequent infections. Such studies have been carried out on asthmatic children, an aged population, and leukemic patients.

Pertussis

A well controlled study has indicated that neither hyperimmune nor normal gamma globulin reduced the incidence or severity of whooping cough when treated subjects were compared with controls injected with gelatin.

In conclusion, immune human gamma globulin is proving itself the most effective means of passive immunization so far devised. However, more effective means and programs for active immunization may obviate its use in many common infectious diseases.

(The many references may be seen in the original article.)

A ROENTGEN SIGN IN STRANGULATING OBSTRUCTIONS OF THE SMALL INTESTINE*

Allan G. Schmidt MD, Radiology 85(4): 698-701, October 1965.

Little has been written lately about the significance of soft fecal material in the cecum and right colon as a sign of strangulated closed-loop obstruction, when associated with the usual roentgen findings of mechanical small bowel obstruction. Recent cases at the Los Angeles County Harbor General Hospital, illustrating this sign, have prompted a review of both the literature and the available radiographs in small intestinal obstruction.

Frimann-Dahl [1] stated, in relation to strangulated small intestinal obstruction, that the colon can occasionally be moderately distended and contain some fecal masses. The gas accumulation is usually seen in severe cases, and secondary peritoneal irritation may play a part. The general rule, however, is for the small intestine and colon to be empty and contracted distal to the obstructive site without evidence of gas or fluid.

Mellins and Rigler [2] included as one of their 10 criteria for strangulating obstruction of the small intestine the presence of moderate amounts of gas in the colon, despite the apparent evidences of small intestinal obstruction.

Eisenman [3] described gas and fecal material in the right colon as a readily detectable finding, which, when associated with the appearance of small bowel obstruction, suggests the possibility of strangulation.

* From the Department of Radiology (AGS Resident), Los Angeles County Harbor General Hospital, Torrance, Calif., and the UCLA Medical Center, Los Angeles, Calif.

Mechanism

Strangulation occurs when the two limbs of a bowel loop with its mesentery are incarcerated so that the mesenteric vessels are compromised. The tighter the strangulation the more fluid and less gas are seen within the closed loop. This accounts for the often minimal x-ray changes. The pseudotumor [6] is most often located in the lower part of the abdomen and on the right side. The intestine can be completely paralyzed, with propulsion no longer present. Perhaps the location of the gangrenous bowel segment and of the paretic intestine explains the failure of the right colon to empty in strangulated small intestinal obstructions. Another factor might be the common blood and nerve supply to the small intestine and right colon.

Discussion

Seventy-five cases of surgically treated small intestinal obstruction seen in the period from July 1963 to December 1964 at the Los Angeles County Harbor General Hospital were reviewed. Nine cases proved to be strangulated small bowel obstructions, and re-examination of the radiographs was possible in 8. All but one demonstrated moderate to marked amounts of soft fecal debris in the right colon. The other presented as a small bowel obstruction with gas-distended loops of small bowel over the cecum.

The finding of bubbly-appearing fecal debris in the cecal-ascending colon region, with gas-distended loops of small bowel and the rest of the colon usually empty, proved strong evidence of strangulated closed loop obstruction. This material did not exhibit air-fluid levels but remained essentially unchanged in the erect or lateral decubitus films. The appearance was similar to that of an abscess, but the shape and location conformed to the cecum. In follow-up abdominal films, if the diagnosis had not been made, there was little or no change in the appearance of the right colon from previous films. This occurred even though the other signs of mechanical small bowel obstruction might have increased and one would normally expect the colon to be empty. The findings should further strengthen the suspicion of strangulated obstruction.

In roentgenograms where strangulation was present and little small bowel gas was seen, the fecal debris with the rest of the colon empty was readily detected. The other signs of strangulation such as the closed loop in the form of the coffee-bean [5] or pseudotumor shadows, were not always demonstrated or identified. Fixed loops can occur with most inflammatory processes, and long fluid levels were not seen when there was little gaseous distention.

This sign was a particularly accurate finding in differentiating simple from strangulated obstructions, as only 3 of 46 cases of simple mechanical small bowel obstruction in this series demonstrated marked fecal debris in the cecum. These, in each instance, were of a more complicated nature. One was an ileal ulcer with perforation and obstruction due to ectopic gastric tissue. The second was a small bowel obstruction with generalized carcinomatosis involving the small bowel and colon. The third was a mechanical obstruction of long duration in which a gangrenous segment approximately one foot long was resected, although no closed loop was identified.

Case Reports

In most instances adhesive bands are the cause of both simple and strangulated small bowel obstruc-

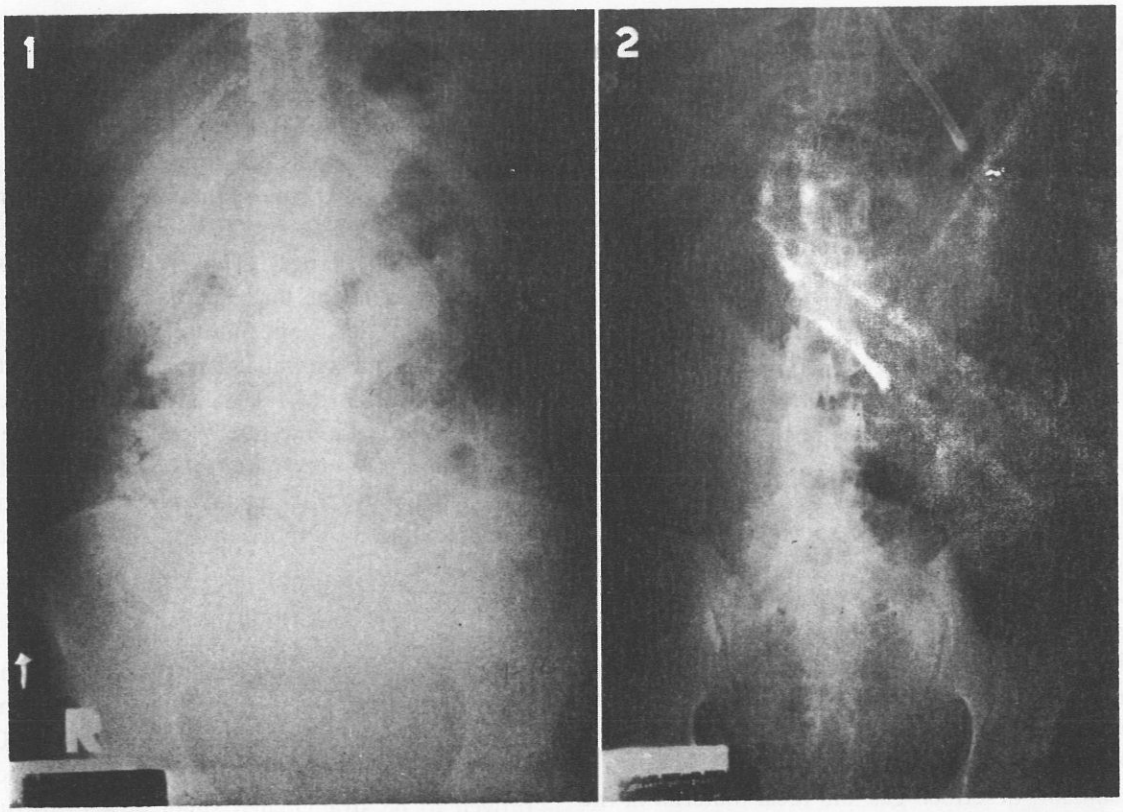


Fig. 1. The erect film, part of the abdominal series, reveals distended small bowel loops and debris in the right colon.

Fig. 2. A supine film forty-eight hours later again reveals distended small intestinal loops with persistence of the fecal material in the right colon. The enlarged uterus containing the fetal skeleton is also identified.

tions. Only one of the strangulated obstructions was from other causes, that being multiple polyps of the Peutz-Jeghers syndrome with production of intussusception and volvulus.

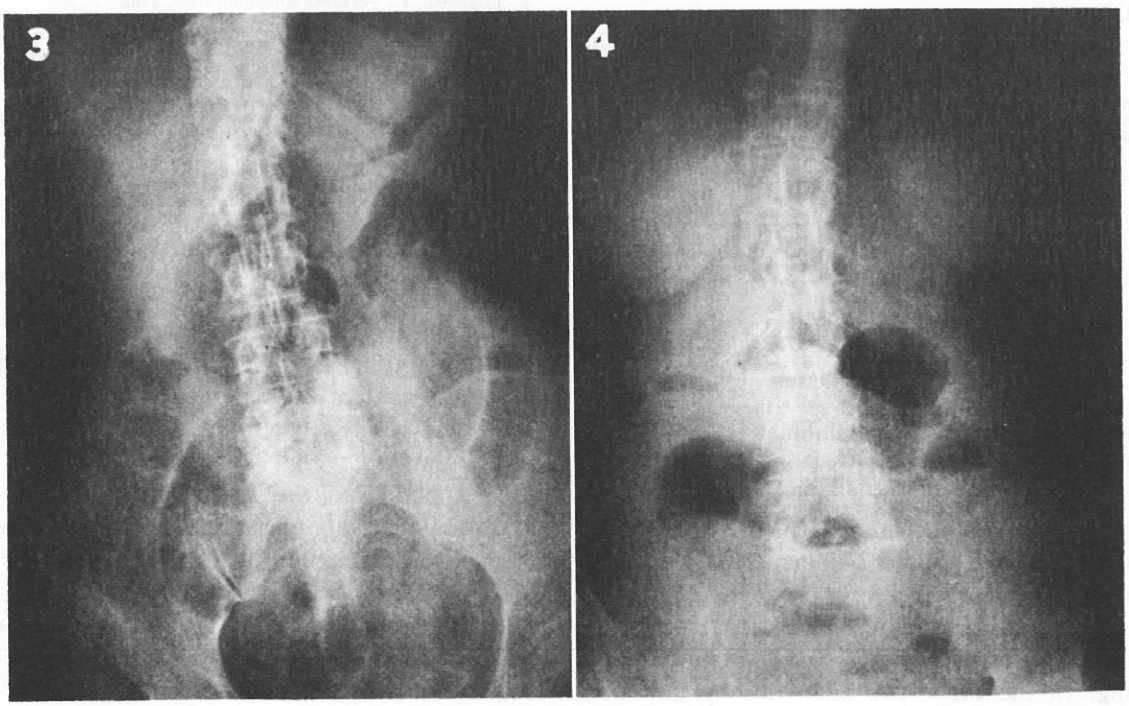
Case I: G. C., a 22-year-old white woman, was admitted because of the sudden onset of midabdominal pain two hours previously. The patient was approximately four months pregnant. X-ray films obtained on admission and forty-eight hours later are shown in Figures 1 and 2. At surgery approximately 1½ ft of ileum was seen under a tight band and twisted. An ileo-ascending colostomy was undertaken. The pathological report was a gangrenous segment of ileum following volvulus.

Case II: G. B., a 58-year-old white woman, awoke with crampy lower abdominal pain; nausea and vomiting developed (Figs. 3 and 4). At surgery the next day approximately 2½ ft of distal small bowel were found under a dense adhesion, resulting in gangrene. Resection of the gangrenous segment and proximal right colon with an ileo-ascending colostomy was undertaken. The specimen disclosed an ileum containing a Meckel's diverticulum, both gangrenous.

Case III: R. M., a 6-year-old white boy, was admitted with a history of intermittent periumbilical pain for the past year. Further distention occurred, and surgery was performed the next day (see Figs. 5 and 6, part of the acute abdominal x-ray series). A closed-loop obstruction was found, secondary to a midgut volvulus of an intussusception. The pathologic report described 3 polyps which demonstrated hemorrhagic infarction in a segment of ileum (Peutz-Jeghers syndrome), together with hemorrhage and necrosis of the mucous membrane of a segment of the ileum, following intussusception and volvulus.

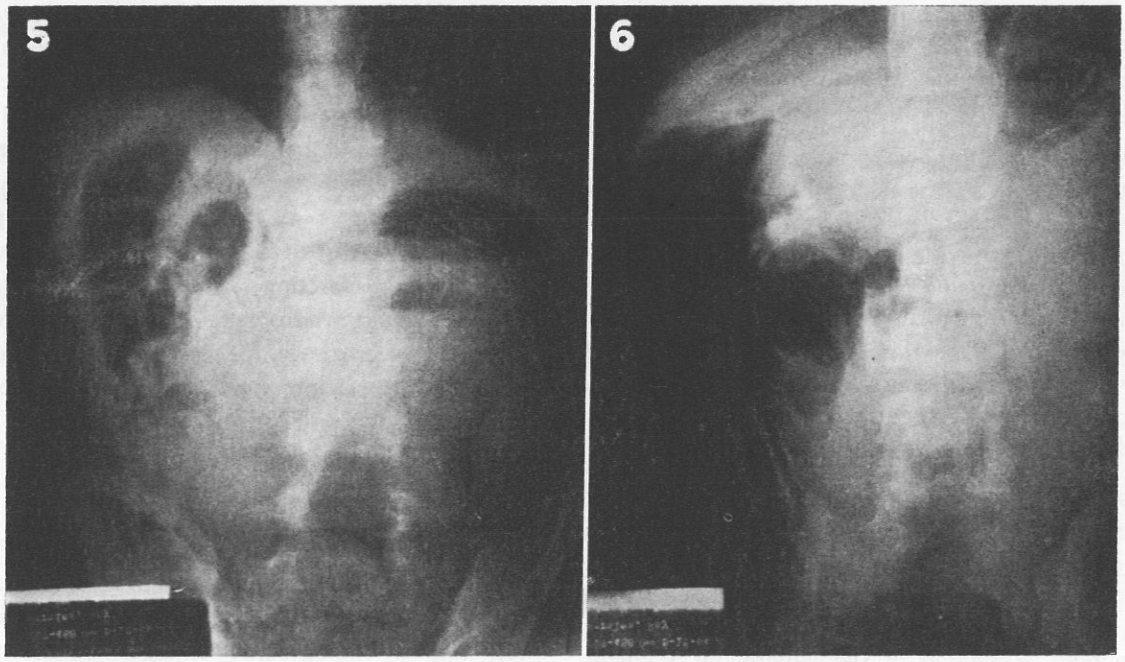
Summary

Seventy-five cases of small intestinal obstruction were reviewed. A readily detected sign of fine fecal debris in the right colon, when associated with the well known radiographic changes in mechanical small bowel obstruction, has been demonstrated in 7 out of 8 cases of strangulated closed-loop obstructions. The author suggests a search for this sign in conjunction with the other roentgen criteria in sus-



Figs. 3 and 4. Case II

Supine and erect films on admission reveal multiple level, air-fluid levels in distended small bowel with the associated fecal debris in the right colon.



Figs. 5 and 6. Case III

Erect and left lateral decubitus films of the abdomen demonstrate the mechanical small bowel obstructive pattern with the fecal debris in the cecum and ascending colon. The pseudotumor is also delineated.

pected cases of small intestinal strangulated obstructions.

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FROM THE NOTE BOOK

SPINACH

Methemoglobinemia

Spinach-induced methemoglobinemia in infants has been previously reported (Clin-Alert No. 308, 1964). The present authors reviewed 14 cases of methemoglobinemia due to spinach. In 12, ingestion of spinach had taken place 24 hours after its preparation. On previous days spinach prepared by the same method had been well tolerated, suggesting that the prepared spinach had produced nitrite on standing. In the other two cases the spinach had been prepared only a few hours before ingestion; the raw spinach must have contained nitrite. A high nitrate content in spinach is a prerequisite for marked nitrite formation. Fresh spinach, frozen spinach, and baby-food spinach, contained an average of 40 to 180 mg nitrate/100 Gm. On incubation at 37° C, nitrate content decreased within 24 to 48 hours, while the nitrite content sometimes became markedly elevated. An increase in bacterial count usually paralleled the formation of nitrite. After a certain interval, nitrite was further degraded to amines and ammonium hydroxide. The coincidence of several circumstances—spinach rich in nitrate as a starting point, type of preparation (use of boiled water), contamination with nitrate-reducing bacteria, and ingestion at a time when nitrites have been formed but not yet degraded, can result in severe poisoning.—Sinios & Wodsak (Hamburg), Dtsch med Wschr 90: 1856, October 15, 1965.* No. 300, November 16, 1965.

MECLIZINES-CYCLIZINES

Teratogenicity

Clinical Study: Observations were made on approximately 8,000 pregnant women of whom 360 received meclizine or cyclizine and 513 "other" antinauseants. No antinauseant drugs were prescribed for the remaining 7,267 patients. The abortion and perinatal mortality rates and the percentage of infants born with nontrivial and severe anomalies among patients receiving meclizine or cyclizine compared favorably with such rates and percentages among patients receiving "other" antinauseants and those receiving no antinauseant drugs. According to these investigators, ". . . it is possible to conclude with reasonable assurance that meclizines in the doses usually prescribed to gravidas are not teratogenic for man."—Yerushalmy & Milkovich (Berkley, Calif), Am J Obst & Gynecol 93: 553, October 15, 1965. [Note: Meclizine is available as Antivert, Bonadoxine, Bonine and Bonamine; cyclizine as Maredox and Merezine. "Other" antinauseants referred to by the authors included Benectin, Bucladin, Combid, Compazine, Dramamine, Emetrol, Mornidine, Tigacol, Tigan and Torecan.]

Laboratory Study: Meclizine and chlorcyclizine hydrochloride ('Di-Paralene'; 'Perazil') are not only teratogenic in the rat, but they also induce the condition of hydramnios. Since the condition of oligohydramnios and polyhydramnios are associated with human congenital malformation, especially cleft palate, it was decided to determine whether the teratogenic effects of these drugs are mediated via induced hydramnios. It has been previously demonstrated that the condition of hydramnios can be directly attributed to the antihistaminic activity of meclizine. Results of the present investigation indicate that the excessive accumulation of amniotic fluid induced by meclizine was not responsible for observed malformations. Both meclizine and chlorcyclizine hydrochlorides are converted to norcnlorcyclizine in mammalian species. The metabolic product is inactive as an antihistaminic but is in itself a strong teratogen in the rat.—King et al. (Bethesda, Md), Am J Obst & Gynecol 93: 563, October 15, 1965.

FDA Label Warning: The Food and Drug Administration has ordered a strong label warning on over-the-counter preparations containing chlorcyclizine, cyclizine, or meclizine or their salts. Labels will bear the statement:

> "Warning—not for use by women who are pregnant or who may possibly be pregnant, unless directed by a physician, since this drug may have the potentiality of injuring the unborn child."

The labeling of prescription preparations containing the above drugs must state that the agents cause defects in animal embryos and that clinical data, while inconclusive, indicate the same possible risk to the human fetus. Information provided physicians must also make it clear that the drugs' effectiveness in preventing nausea in pregnancy "has not been established."—Federal Register 30(208): 13628, October 27, 1965.—Clin-Alert No. 289, November 16, 1965.*

ESTABLISHMENT OF A HEALTH CARE ADMINISTRATION JOURNAL CLUB

A Health Care Administration Journal Club was established at the U.S. Naval Hospital, San Diego, California on 23 September 1965. The purpose of this organization is to aid Medical Service Corps and other interested officers in keeping abreast of current philosophies and practices in the field of Health Care Administration.

During the weekly luncheon meetings, three members each report on a previously assigned journal. These reports are followed by a discussion period. Time is reserved at the end of each meeting for members to exchange new information and ideas. The Health Care Administration Journal Club has received the enthusiastic support of all concerned. Besides sixteen officers of the Supply and Administration Section of the Medical Service Corps, the membership also includes the Pharmacy Officer, the Legal Officer and the Civil Engineering Corps Officer.—CO, U.S. Naval Medical School, NNMC, Bethesda, Maryland.

SULFONAMIDES

Stevens-Johnson Syndrome

Attention has been previously directed to the occurrence of the Stevens-Johnson Syndrome (a serious variety of erythema multiforme) in patients receiving sulfonamides, especially sulfamethoxypyridazine ('Kynex'; 'Midicel'; 'Lederkyn'; 'Retasulfin'). The Australian Director-General of Health reports three additional cases of this drug-induced syndrome. (Nineteen cases have been previously recorded in Australia, with four deaths.) Two of the recent cases occurred with sulfamethoxypyridazine and one in association with sulfamethoxydiazine ('Durenate'). It should be noted that this serious reaction is not confined to the long-acting sulfona-

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mides. Seven cases of the Stevens-Johnson Syndrome were reported to the Australian Drug Evaluation Committee during a 12-month period (Aug 1964–1965) in association with a number of short-acting sulfonamide drugs.—Refshauge (Canberra, Australia), M J Australia 2: 549, September 25, 1965. Republished from Clin-Alert No. 295, November 16, 1965, by permission of Science Editors, Inc.

THE AFFLUENT PHYSICIAN?

Physicians in the United States, with an average annual income in the neighborhood of $17,000, head the list of the leading professions in terms of receipts. They are assumed therefore to be in the best financial position and, by many, in the least need for support during their period of graduate training.

Few graduates of medical schools agree with this popular impression, yet not all are equipped with sufficient facts to furnish a rebuttal. Although it has been pointed out repeatedly that the costs of a medical education exceed those in graduate areas of arts and sciences (and that students of medicine receive about one-fourth as much aid in the form of nonrefundable grants), re-examination of the data may give new insight and more convincing arguments.

Let us look at the average M.D. at 1 point in time—that point at which he is in a position so that his income might exceed expenses. At this juncture he is thirty-one years of age, married, and the father of at least 1 child. He has completed an internship, served in the capacity of a resident for two years, taken two additional years of special training or served in the armed forces, and in but another year may be in a position to qualify for his specialty board examinations.

He is already $600 in debt in the form of loans which must eventually be repaid, and there are small additional interest charges. In addition, he has furnished a home and the likelihood that he has indulged in credit buying for furnishings, a mortgage, or an automobile is great. He has yet to furnish and equip an office. Beyond his medical school expenses were his family living costs—some obligatory obstetrical and medical expenses, the acquisition of some life and other insurance, and additional essential items. Considering the fact that his medical school expenses averaged about $3,000 per year if he was single, $5,500 if married, and that his subsequent annual budget as head of a family could scarcely be less, it is fair to say that the average physician does not reach his "break even" point until about the age of thirty-three unless he has independent means.

Put another way, and with the assumption that the average retirement occurs at age sixty-five, the physician has eight less years of earning power than does a graduate with a doctorate in the arts or sciences or with a professional degree other than an M.D.—a 25 per cent reduction in working years. With this correction, the average annual income of the practicing physician does not tell the whole story.

All medical schools are in need of additional funds in the form of nonrefundable student grants, and many young physicians find themselves in jeopardy because of the financial stringency of their early postgraduate years—their marital adjustments, security, happiness, and even their educational opportunities and career choices, are often at stake. It is up to the medical profession to voice the problems of medical education and practice. It is up to the medical profession to interpret the facts correctly to a public upon whose help we must rely.—George A. Perera, MD, Associate Dean, Columbia University, College of Physicians and Surgeons. J Med Education 40(11): 1085, Nov., 1965.

DENTAL SECTION

INDIRECT PULP CAPPING: A BACTERIOLOGIC STUDY OF DEEP CARIOUS DENTINE IN HUMAN TEETH

King, J. B. Jr., Crawford, J. J. and Lindahl, R. L. Oral Surg, Oral Med, and Oral Path. 20(5): 663–671, Nov 1965.

During restorative treatment it is customary to remove all decalcified and stained dentine from deep carious lesions, thus risking exposure of the pulp. However, there have been many reports of the successful use of the indirect pulp-capping method. The purpose of this investigation was to determine whether the soft residual layer of carious dentine in teeth treated by the indirect pulp-capping method is contaminated with cultivable microorganisms prior to treatment; and whether this layer, if contaminated, could be rendered sterile by capping with either calcium hydroxide or zinc oxide and eugenol.

Using pedodontic patients, fifty-one deeply carious, vital, asymptomatic teeth were studied in vivo. The indirect pulp-capping technique was performed under aseptic conditions utilizing the test materials as follows: 21 teeth were capped with calcium hydroxide, 22 with zinc oxide and eugenol, and 8 with silver amalgam as controls. Bacteriological samples were taken from the deepest layer of intact carious dentine of each tooth before placing the test materials. The teeth were then restored with silver amalgam.

The teeth were reopened 25 to 206 days later, bacteriological samples were taken again, and remaining carious dentine was removed. Only 3 pulp exposures ensued, and these were from the 8 amalgam controls. The bacteriological cultures were of both the broth and agar plate types. All pre-capping broth cultures were positive. Upon reopening, the following broth culture results were obtained: 13 of 21 (61.4%) teeth treated with calcium hydroxide were negative; 18 of 22 (81.8%) teeth treated with zinc oxide and eugenol were negative; all 8 silver amalgam controls were positive. All but 2 pre-capping agar plate cultures were positive. Upon reopening, the following agar plate culture results were obtained: 13 of 16 (81.2%) teeth treated with calcium hydroxide were negative; 16 of 21 (76.2%) teeth treated with zinc oxide and eugenol were negative; all 8 silver amalgam controls were positive. The agar plate cultures also indicated a general reduction in the number of cultivable microorganisms in the treated lesions.

It is evident from these results that the deep layer of residual caries is usually contaminated with cultivable microorganisms; and that this layer can be sterilized, or that the number of organisms can be greatly reduced when this layer is capped with either calcium hydroxide or zinc oxide and eugenol.

(Abstracted by CDR W. B. Gregory Jr. DC USN, U.S. Naval Academy, Annapolis, Maryland.)

EFFECT OF SURGICAL EXPOSURES OF DENTAL PULPS IN GERM-FREE AND CONVENTIONAL LABORATORY RATS

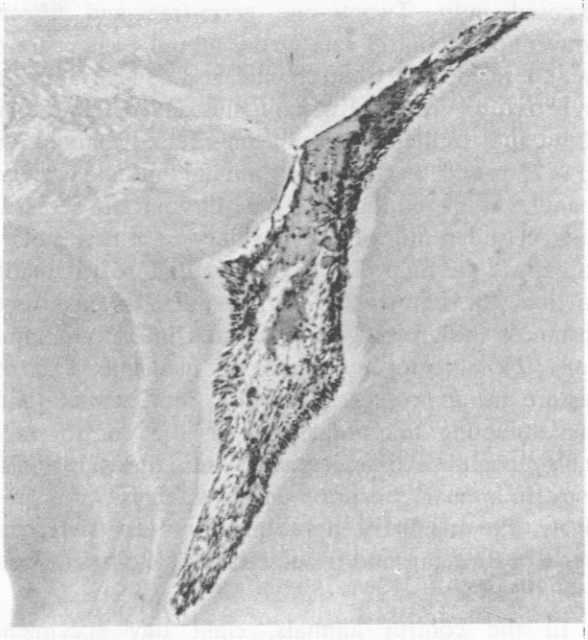
Kakehashi, S., Stanley, H. R. and Fitzgerald, R. J. Oral Surg, Oral Med and Oral Path. 20(3): 340–349, 1965.

Histological study of pulp response to surgical exposure in germ-free animals contained in the germ-free environment of a Reyniers System Unit was used to demonstrate conclusively the influence of viable microorganisms on the fate of the surgically exposed pulp. Twenty-one germ-free and fifteen conventional control rats of the inbred Fisher strain were studied. The experimental and control animals were fed an identical diet of autoclaved laboratory chow and distilled water. In anesthetized animals, a #1/2, round, carbide bur mounted in a jeweler's mandrel was used to drill a hole through the occlusal enamel and dentin of the maxillary right first molar, to expose the pulp tissue. Although effort was made to limit the bur to the coronal pulp, in numerous instances the crown was penetrated laterally or apically. No attempt was made to medicate, seal or restore the exposures. Therefore, food debris (and contaminating microorganisms in the control animals) could become impacted into the pulpal tissues. In animals sacrificed one to 42 days postoperatively, the maxillary right quadrant was removed, fixed in formalin and processed for histological examination.

In the control animals, eight day specimens showed vital pulp tissue remaining only in the apical half of the roots; the remaining coronal half of the pulp was necrotic, purulent and usually contained microorganisms; and the occlusal cavitations were packed with food and debris. In all control specimens beyond the eighth day, complete pulpal necrosis had occurred, and chronic inflammatory tissue and abscess formations were seen in the apical areas. A few specimens showed microorganisms in the soft tissues beyond the apical foramen. Abscesses were also found at accessory foramina. In no instance was evidence of repair seen in the injured pulpal tissues. Especially lacking were matrix formation and attempted dentinal bridging.

In the germ-free animals, despite pulpal exposures including gross perforations, no completely devitalized pulp was observed. In every specimen, the pulpal inflammation was minimal. Not a single apical abscess was found. Dentinal bridging was evident at 14 days, with prominent quantities of matrix formation. Older specimens showed matrix formation completely bridging or sealing the exposure. In every instance, the pulp tissue remained vital beneath the reparative dentinal bridge. The bridging occurred at any angle, regardless of the angle or severity of the exposure. With increasing postoperative time, a gradual constrictive obliteration of the pulp chamber, with new matrix containing many cellular inclusions, was observed. Sometimes even accessory canals in the apical root area showed constriction by matrix formation.

In these experiments, conditions were deliberately chosen to compare the effects on pulp healing of op-



Photomicrograph—32 day postoperative germ-free specimen. Note completion of bridge with vital, non-inflammed pulp tissue remaining.

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posite extremes of the microbiological environment, namely the complete absence of all bacteria versus a grossly contaminated environment. Secondly, no attempts were made to influence the course of the reparative processes by any therapeutic measures. Under these conditions, in spite of severe surgical trauma complicated by impaction of food and debris, the germ-free pulps exhibited recovery and a reparative response. These results conclusively demonstrate the importance of measures for eradicating all bacteria in effective clinical management of exposed pulps.

STUDIES OF A FAMILY WITH THE ORAL-FACIAL-DIGITAL SYNDROME

Doege, T. C., Thuline, H. C., Priest, J. H., Norby, D. E. and Bryant, J. S. New Eng J Med 271: 1073–1080, Nov 19, 1964.

The oral-facial-digital syndrome (characterized by cleft tongue and jaw, cleft lip and palate and digital malformation) has been found in 15 females, in four generations of one family.

The family's ancestry was traced to Scotland, where members of generations I and II were born. Fifteen affected females and no affected males were born in generations II to V in seven western states of the United States. The entire family included 78 live births and 13 abortions. Six of the normal males born to affected females have had offspring; the syndrome has not occurred in any of the 10 daughters and 9 sons of these men.

The constant clinical features of the trait in the family included a typical profile with a narrowed upper lip and pug, hooked nose and cleft tongue. Also present are lateral tori of the maxilla, giving the appearance of a pseudocleft, and multiple, abnormally positioned, multitufted buccal frenula. Yellowish tumors of the tongue and skin are generally present. Five of six affected females given psychologic tests were mildly retarded. Other clinical features include cleft palate, brachydactylia, syndactylia, polydactylia and clinodactylia. Less frequent abnormalities are cleft alveolar ridges, cleft lip, incomplete cleft lip, abnormally positioned teeth and scanty hair.

The findings suggest that the syndrome is inherited as either a sex-linked or an autosomal dominant trait, with lethality in males in either instance.

ADHESIVE POWDERS FOR DENTURES

Tiecke, R. W. JAMA 191:876, Mar 8, 1965.

Denture adhesive powders are made from finely powdered vegetable gums such as karaya or synthetic substances with small amounts of essential oils, plus up to 12 percent of sodium borate added to neutralize the acidity of the karaya.

There have been no reports of borate toxicity from use of denture adhesives, but a nonborate preparation might be recommended for use by patients with impaired renal function.

A more frequent danger is the improper use of a denture adhesive in order to tolerate an illfitting denture that may injure the supporting tissues.

(D ABS 10(7): 417, July 1965. Copyright by the American Dental Association. Reprinted by permission.)

PERSONNEL AND PROFESSIONAL NOTES

DENTAL OFFICERS PRESENTATIONS. CAPT V. J. Niiranen DC USN, Assistant Chief of the Dental Division, BuMed, presented a lecture entitled Dental Medicine Support of Marine Corps in Viet Nam, before medical and dental students of Tufts University on 13 November 1965 in Boston, Massa-

chusetts. The lecture was part of a symposium entitled What's New in Military Medicine, in support of the Medical Education for National Defense (MEND) program, a Joint Armed Forces effort.

CAPT Niiranen portrayed the role of the Navy and Marine Corps personnel deployed in South-East Asia with emphasis on the field dental support to the Marine Corps in the Republic of Viet Nam, and the professional contributions by dental personnel to the Vietnamese people as part of the civic action program.

CAPT J. F. Link DC USN, U.S. Naval Hospital, Great Lakes, Illinois, presented a paper and slide demonstration entitled This Fracture Business before the Oral Surgery graduate students at Loyola University School of Dentistry on 10 November 1965 in Chicago, Illinois.

LCDR H. J. Keene DC USN, 5th Dental Company, 1st Marine Brigade, FMF, presented a table clinic entitled Periodontal Disease in Caries Resistant Naval Recruits, before the Pacific International Dental Conference on 17 November 1965 in Honolulu, Hawaii.

PREVENTIVE MEDICINE SECTION

DYSENTERY OUTBREAK AMONG MARINE CORPS PERSONNEL, VIETNAM

A Marine Corps Unit stationed in Vietnam recently experienced an outbreak of dysentery with an overall attack rate of 17.5%.

Symptomatology consisted of a sudden onset of cramps followed immediately by diarrhea. Stools were occasionally mucus-flecked and some contained pink blood. Low grade fever, nausea, and vomiting were common.

The majority of patients responded well to symptomatic therapy; severely ill patients were given IV fluids and antibiotics. It was reported that tetracycline (250 mg QID X 5d), Gantrisin (6 gms stat, then 4 gms QD X 4d), or Neomycin (250 mg QID X 5d) were all effective in relieving the symptoms.

Examination of stools of both asymptomatic food-handlers and patients revealed a significant number positive for *Shigella flexneri*.

Epidemiological investigation disclosed that two food items, baked spam and/or ice cream, were most suspect vehicles. Unfortunately, no food was available for laboratory analysis. Of interest, however, is the fact that 2 asymptomatic cooks were found to have *S. flexneri* in their stools at approximately the same date the suspect meal was served.

Inspection revealed that water was not the suspect vehicle since other units employing the same source had not experienced increased diarrheal disease.

However, several fly breeding areas were noted around latrines and in moist areas below the galley. Insecticiding by Preventive Medicine Unit personnel has reduced the fly density but permanent control will depend as always, upon proper construction of fly-proof latrines, construction of screened garbage shacks, adequate drainage for galley wastes (particularly grease), adequate hand washing facilities in the galley, and a continuous insect spraying program by medical department personnel.

Immediate control of the outbreak was by treatment of all patients and screening of food-handlers. It was suggested that patients treated with sulfa, or who relapse, be re-examined and retreated immediately if found positive.

This outbreak presents several interesting features:

(1) The common occurrence of vomiting.

(2) Symptomatic therapy was apparently moderately effective.

(3) Gantrisin was of value in the treatment of severely ill patients. Most strains of *S. flexneri* isolated from military patients in the United States have been solidly resistant to sulfa drugs *in vitro* and *in vivo*.—PrevMed Div, BuMed.

DENGUE TYPE 2 VIRUS IN NATURALLY INFECTED *AEDES ALBOPICTUS* MOSQUITOES IN SINGAPORE

Rudnick, A. and Chan, Y. C., Science, 149(3684): 638–639, Aug 6, 1965.

Mosquito-borne hemorrhagic fever is a severe clinical syndrome etiologically associated with strains of dengue virus and newly recognized in southeastern Asia and India (Hammon, et al; Sarkar, et al, WHO Regional Office). During an inves-

tigation of the first recognized outbreak of the disease in Singapore in 1960–61 (Chew, et al; Lim, et al), strains of dengue virus were isolated from the serums of 2 patients (Lim, et al), 5 pools of *Aedes aegypti* mosquitoes, and 1 pool of *A. albopictus* mosquitoes. Of the 2 viruses isolated from patients, 1 was identified as type 1 dengue and the other as type 2 dengue. All of the virus isolates from mosquitoes proved to be type 2. This is the first report of an isolation of dengue virus from naturally infected *A. albopictus*, a proven efficient experimental vector of dengue (Simmons, et al) and long suspected as a vector in nature on epidemiological grounds (Lumley, G. F., Smith, C. E. G.).

Although *A. aegypti* has been incriminated as the principal vector of dengue for many years, it was not until 1960 that the first isolation of the virus from naturally infected mosquitoes was reported (Hammon, et al). At that time, isolations were made of dengue type 3 virus from *A. aegypti* collected in the Philippines in 1956 and of dengue type 2 from *A. aegypti* collected in Bangkok in 1958 during hemorrhagic fever epidemics. Subsequently, additional strains of virus have been isolated from *A. aegypti* collected in India (Carey, et al), Thailand (Halstead, et al), and South Vietnam (WHO Regional Office). These various isolations include all 4 types of dengue virus. No isolations were made from *A. albopictus*, collected and processed under similar circumstances.

In Nov 1960, following the peak of the epidemic in Singapore, and while cases were still occurring, a mosquito survey was initiated. Adult mosquitoes were taken routinely on a weekly basis from urban and rural houses, in diurnal and nocturnal biting collections, and from animal bait. Twelve thousand five hundred and five mosquitoes, representing more than 40 species of 8 genera, were collected in a 3-month period. Of these, more than 6,000 female mosquitoes were processed for virus isolation.

Collected mosquitoes were held alive for a minimum of 24 hours before being processed, in order to allow for digestion of any freshly engorged blood. They were then lightly anesthetized with chloroform and accurately identified as to species. Female mosquitoes were stored at −70° C. Frozen mosquitoes were pooled by species, date collected, and location. Generally, not more than 50 mosquitoes were included in each pool. The pooled frozen mosquitoes were suspended in 3 ml of diluent (33% normal inactivated rabbit serum in beef heart infusion broth) and centrifuged at 10,000 rev/min for 20 minutes. A portion of the supernatant was treated with a penicillin-streptomycin mixture in the cold, and subsequently inoculated intracerebrally (0.01 ml) and intraperitoneally (0.03 ml) into two liters of 1- to 2-day-old mice. The mice were observed for signs of illness for 21 days. Brains were harvested from all sick mice, and suspended and inoculated into new groups of mice. Where no illness occurred between the 5th and 8th days after inoculation, the brains were harvested from 2 mice and stored.

From 4 to 5 weeks after inoculation, the surviving mice were challenged with doses of approximately 100 LD_{50} of adult-mouse-adapted dengue type 2 (Trinidad 1751) virus. Where dengue-challenge resistance occurred, the stored mouse brains were prepared as 20% suspensions, then diluted to 10%, and inoculated into mice. Portions of all mosquito suspensions and mouse brain suspensions were stored at −70° C. Part of the laboratory work was done in Singapore, where the mice were held in a mosquito-proof room. The remainder of the work was done in San Francisco, a dengue-free area.

Five strains of dengue virus were isolated from *A. aegypti* pools and 1 strain was isolated from a pool of *A. albopictus*. The *A. albopictus* strain (SM–18) was from a pool of 49 females that were collected in Nov 1960 in urban Singapore, while they were attempting to feed on human bait. The dengue virus infection rates were 0.8 per 1,000 for *A. albopictus* compared to 18.6 per 1,000 for *A. aegypti*.

Strain SM–18 caused illness in infant mice 10 days after inoculation with the mosquito suspension, but it adapted to mice with difficulty. Ten serial brain passages in infant mice were required before the incubation period was reduced to 7 days and a regular pattern of illness and death appeared. Of the 52 mice that survived inoculation with SM–18 in the first several passages, 43 survived subsequent dengue challenge, which shows the acquisition of immunity, which, in turn, demonstrates the presence of dengue virus in the original inoculum. Virus strain SM–18 was reisolated successfully in mice from a stored sample of the original mosquito suspension.

The results of intracerebral neutralization tests in mice showed that SM–18 is a strain of dengue type 2 virus. Hyperimmune serums were prepared in adult mice by a series of 5 intraperitoneal inoculations with live virus, and in rabbits by a series of 4 intramuscular inoculations with live virus. Typing by the microprecipitin agar gel diffusion technique (Chan, Y. C.) confirmed the results of the neutralization tests. With SM–18 antigen (a 20% infant mouse brain suspension in borate-saline diluent at

pH 9.0), precipitation occurred only with dengue type 2 and not with dengue types 1, 3, or 4, or with Japanese encephalitis hyperimmune mouse serum. No nonspecific precipitation occurred with normal mouse serum.

It has been established that *A. aegypti* is the primary vector of dengue-caused hemorrhagic fever in southeastern Asia, based on epidemiological evidence and numerous virus isolations. The significance of the single isolation of dengue virus from *A. albopictus* cannot be evaluated without further investigation, although epidemiological evidence suggests that this species is an important vector of endemic dengue in southeastern Asia (Smith, C. E. G.).

TRACHOMA IN THE RYUKYU ISLANDS

Several conflicting reports have appeared concerning the incidence and severity of trachoma in the population of the Ryukyu Islands. In an attempt to clarify the situation, the Government of the Ryukyu Islands invited members of the Naval Medical Research Unit No. 2, Taipei, to conduct a lecture and demonstration program on the diagnosis and treatment of trachoma. In conjunction with the demonstration program, a cross section of the population was examined in order to determine incidence and severity of trachoma and necessary eye swabs and scrapings taken for virus isolation and identification. The team visited the Ryukyu Islands during June, 1965.

The enclosed table summarizes the results of the clinical examinations by age group.

It is evident that any proposed treatment program should be based upon almost double the present estimated 15% rate. Distribution of active cases by age group is similar to the rates reported by the same group in Taiwan and indicate the primary school grades as the most logical starting point for a treatment program.

Laboratory results of trachoma strain isolation and characterization will be presented upon completion of work.—PrevMed Div, BuMed.

RESULTS OF CLINICAL EXAMINATIONS ALL AREAS BY AGE GROUP
11 THRU 22 JUNE 1965, RYUKYU ISLANDS

Age Groups	No. Exam.	N.P.	Foll.	S.C. C.F.C.	N.D. Tr.D.	Tr. I	Tr. II	Tr. III	Tr. IV	A.C.	% Active Less Dubium	% Active Plus Dubium	% Inactive Trachoma
0–5	10	3	2	2	1	1	0	0	0	1	10%	10%	0.0%
6–10	560	53	143	174	55	56	69	4	5	1	23.0%	32.8%	0.9%
11–20	180	17	37	46	21	8	38	3	10	0	27.2%	38.9%	5.5%
21–30	45	10	3	6	1	0	8	4	13	0	26.7%	28.9%	28.9%
31–40	27	7	1	1	1	0	6	2	9	0	29.6%	33.3%	33.3%
Over 40	67	9	3	3	0	0	4	13	35	0	25.4%	25.4%	52.2%
TOTAL	889	99	189	232	79	65	125	26	72	2			

KEY TO ABBREVIATIONS:

N.P. = No pathology
Foll. = folliculosis
S.C. = Simple conjunctivitis
C.F.C. = Chronic follicular conjunctivitis
N.D. = Non-determined
Tr. D. = Trachoma dubium

Tr. I = Trachoma stage 1
Tr. II = Trachoma stage 2
Tr. III = Trachoma stage 3
Tr. IV = Trachoma stage 4
A.C. = Acute conjunctivitis

LEPTOSPIROSIS—U.S. 1965

Va Dept of Hlth, Morb Rpt for the Week Ended 23 Oct 1965.

Leptospirosis is not a common human disease in the United States. It occurs in all sections of the country and may be acquired from a wide variety of domestic and wild animal hosts. The reported human cases has more than doubled during the past decade. This may be attributed to an increasing awareness that the disease is not limited to the severe icteric illness characteristic of Weil's syndrome but is more frequently mild and anicteric. In addition, improved procedures in laboratory diagnosis for the

detection of leptospiral infections have become more widely available.

In cattle, leptospirosis is a major problem. The disease is also prevalent in swine and dogs, but it occurs infrequently in most other domestic animals. Human cases are commonly traced to direct or indirect contact with these domestic animals.

Knowledge of the wide distribution of leptospirosis in wildlife species has expanded greatly during the past decade. Attention can no longer be focused on rodents alone since a wide variety of both wild and domestic mammals can serve as important hosts. For many species, such as skunks, opossums, raccoons and foxes, the finding of infection rates of 10–50% is not uncommon. Leptospires have also been found in a few instances in birds, reptiles, turtles and ticks.

Information on human cases was obtained from 2 sources:

a. 928 human cases were reported to the National Office of Vital Statistics and to the Communicable Disease Center, Atlanta by State health departments from 1947 through 1964.

b. 601 cases occurred in the continental United States during the same 18-year period and 44 cases that occurred in Hawaii from 1962 through 1964. Laboratory diagnosis in 407 of these cases was confirmed at CDC, in 168 at the Walter Reed Army Institute of Research, Washington, D.C., and in 71 at State health department laboratories.

Attack rates for the 830 cases from the United States (excluding 98 cases from Hawaii) ranged from a low of 0.1 to a high of 4.5 cases per 100,000 population. (Virginia, 0.55) It should be emphasized that the reported number of cases represent only a portion of the actual number of cases.

The annual occurrence of reported cases (excluding Hawaii) increased from 14 in 1947 to 83 in 1959, followed by a decline through 1963. (In preliminary reports for 1964, however, the number of cases nearly doubled those for the preceding year.)

Of the 601 cases in the Continental United States, 70% had onsets from June through Oct with the highest occurrence in Aug. Age was known on 456 of the 601 cases. Of these 456, 339 (74%) were between the ages of 10 and 50 with the highest number (105, 31%) in the 30–39 year age group. Five hundred and thirty (88%) of the 601 cases were among males. Information as to occupation was available in 461 of the 601 cases. The occupation in 142 (31%) of the cases involved direct contact with potentially infected animals in farming, abattoir work, veterinary work or other work with animals. Exposure in children frequently involved swimming in contaminated waters or direct contact.

The probable place of infection was determined in 378 of 601 cases. The greatest proportion of cases occurred on farms in abattoirs, or in handling domestic animals (142 cases, 38%) or in the home (88 cases, 23%). Eighty-six (23%) involved water contact either in the course of the patient's occupation or while swimming in contaminated ponds or streams.

Of the 378 cases, an infecting source could be determined in 241; 85 cases (35%) involved contact with cattle or swine, 72 (30%) with rodents, 71 (29%) with dogs, and 8 (3%) with other animals. Seven of the 8 cases which involved contact with other animals were exposed to raccoons, opossums or rabbits while hunting. One was exposed to a goat. Seven infections resulted from contact with leptospires in the laboratory; 5 patients were directly exposed and 2 were infected through contact with laboratory animals.

For some cases, the diagnosis of leptospiral infection was confirmed in the animal contact or illness was observed in the animal. (In most instances identification of the probable animal source was presumptive.) Most of the infections from cattle and swine occurred on the farm or in the abattoir (75 of 85 cases, 88%). The majority of infections from dogs occurred in the home 52 of 71 cases, (73%) although 12 of 71 cases (17%) resulted from contact during veterinary work. Infections from rats took place in a wide variety of places.

FOOD POISONING EPISODE DUE TO SHIGELLA

L. A. County Hlth Index, 18 Sep 1965.

Between 700 and 900 cases of shigellosis are reported yearly in Los Angeles County. This is approximately double the number of reported cases of salmonellosis. While "food poisoning" outbreaks due to *Salmonella* are common, recognized food-borne infections due to *Shigella* organisms are infrequent. No food-borne outbreak in which *Shigella* was the recognized etiologic agent has been investigated by the Los Angeles County Health Department during the past 10 years.

Earlier this summer a report was received of

diarrheal illness in 3 children. Subsequent investigation revealed that these children were part of a group of more than 100 people who had attended a wedding reception. The reception had been held at the home of the bride's family and the food had been prepared by the various family members of both the bride and the bridegroom.

Many of the guests had been invited by word of mouth and difficulty was encountered in determining the identity of those who had attended. Continued questioning eventually yielded information from 77 guests and from 2 additional persons who did not attend. These 2 ate food brought to them from the reception. Seventy of this group of 79 persons reported symptoms of illness.

Sixty percent reported diarrhea and cramps, 50% fever and approximately 30% reported nausea and vomiting. Among the children and in some of the adults, as many as 10 or more watery green stools per day were reported, with the diarrhea lasting for one to two days. Temperatures of 100° F. to 105° F. were reported by several of the victims. Recovery usually took place in 2 to 4 days.

The minimum incubation period reported was 6 hours and the maximum 6 days. The median figure was 40 hours. Fifty percent of the incubation periods fell within a range of 30 hours to 48 hours. The longer incubation periods probably represent secondary cases.

Stool specimens from 4 persons who attended the reception were positive for *Shigella boydii*, serotype 2. Three children in a family whose parents attended the reception and were subsequently ill, became ill of a diarrheal illness 2 days, 5 days, and 9 days, respectively, following illness in the parents. Stool specimens from 2 of the 3 children were positive for *Shigella boydii*, serotype 2. In another family, 3 children who attended the reception and were subsequently ill with diarrheal illness, had stool specimens negative for *Shigella* organisms. However, a playmate who had not attended the reception became ill with a diarrheal illness approximately 2 weeks following the onset of illness in these 3 children. A stool specimen from this child was positive for *Shigella boydii*, serotype 2.

Nineteen families in 9 communities were represented by the victims from whom information was obtained. The occurrence of a severe diarrheal illness in 85% of the members of this group of families within a period of 3 days following the wedding reception indicates a common source infection. The isolation of *Shigella boydii*, serotype 2, an organism not prevalent in the community, from both victims and persons associated with victims identifies this organism as the etiologic agent.

Nine victims reported that they ate only potato salad. Of these 9, one did not attend the reception but ate the potato salad brought by a guest. Three more reported that they ate only potato salad and stuffed turkey, and one of these 3 had not attended the reception but had eaten food brought by a guest. Five victims denied eating potato salad. Potato salad is implicated as the contaminated food.

The ingredients for the potato salad had been prepared during the evening preceding the wedding reception. They were prepared at the home of the bride by the bride's mother, sister, and the mother of the groom. While so engaged, the 3-year-old daughter of the bride's sister was ill with vomiting and diarrhea. On several occasions it was necessary for one or more to stop their work and care for this child. The epidemiologic history suggests that the child may have been ill with shigellosis and *Shigella* organisms transferred to the potato salad by the food handlers. Shigellosis, however, was not confirmed in this child.

SOURCES OF AIR-BORNE MICRO-ORGANISMS IN FOOD PROCESSING AREAS—DRAINS

Heldman, D. R.; Hedrick, T. I.; and Hall, C. W. Jour of Milk and Food Technology 28(2): 41, February 1965.

The extent to which food plant air may be contaminated with microorganisms from flooding floor drains has been investigated. Results indicate that bacteria counts obtained during flooding may be as high as 140 per ft. in areas where normal counts are usually less than 10 per ft. The air-borne yeast and mold contributions due to flooding were about 6 per ft. compared to a background of 1 per ft., and about 12 per ft. compared to background counts of 4 per ft., respectively. By continuous intermittent flooding, the amount of contamination due to flooding decreases. However, if the drain sets without flooding for a period of one hour, the contribution may be as great as during the first flooding of the day. Results indicated that application of about 5 gallons of a 800 ppm chlorine sanitizer would provide a significant reduction in contribution. A maximum reduction of 87 percent was obtained using a sanitizer concentration of 5,000 ppm.

BACTERIOLOGICAL STUDIES ON THE SHELF LIFE OF SOFT SHELL CLAMS (MYA ARENARIA)

J. R. Cox, Natural Resources Institute, Univ of Maryland, Jour of Milk and Food Technology 28(2): 32, February 1965.

Bacteriological shelf life studies on fresh packed soft shell clams harvested from Chesapeake Bay were conducted at three month intervals to determine the effect of seasonal changes on standard plate counts, 25 C plate counts, coliform most probable numbers, and other microflora in relation to spoilage and discoloration. The data obtained in these studies indicate the following: (a) no correlation between either standard or 25 C plate counts and the degree of spoilage was noted; (b) coliforms multiply in shucked soft shell clams caught in cold waters and stored at 33–35° F., but may decrease during storage when harvested from warmer waters; (c) there may be a slight increase followed by a decrease in E. C.+ and *E. coli* (fecal coliforms) most probable numbers after 5–7 days storage, but when E. C.+ MPN's have been very low or 0 no increase has been found; (d) no correlation between pink yeast counts and pink discoloration of soft shell clams, or between any chromogenic bacteria or other discolorations was noted; and (e) the bacteriological standards for fresh shucked oysters which are based on E. C.+ MPN's (fecal coliforms) and standard plate counts were met although some counts were in the "Acceptable on Condition" classification when sampling was made during summer and early fall.

PROGRESS REPORT ON THE *AEDES AEGYPTI* ERADICATION PROGRAM

Schliessmann, D. J., Vector Control Briefs, HEW PHS, Issue No. 15, p. 7–8, Aug 1965.

Surveys conducted during the spring and early summer of 1965 indicate good possibilities of eradicating the yellow fever mosquito, *Aedes aegypti*, in the states of Louisiana and Arkansas. During the first year of actual field operations, the *Aedes aegypti* index has been reduced in all operational areas.

Funds were approved to begin small-scale eradication activities in Hawaii, where the mosquito is known to occur on 3 islands. The program will be conducted under the direction of the Chief, Vector Control Mosquito Branch, Hawaii Department of Health. Actual field surveys on the Kona Coast of Hawaii began in June 1965.

The number of operational areas was expanded in July from 7 to 16 in Florida, from 3 to 9 in Texas, and from 10 to 16 in Puerto Rico. Summer surveys to define areas for actual eradication operations in the spring of 1966 were conducted in South Carolina, Georgia and Alabama.

Great progress was made in source reduction programs at San Antonio, Laredo, and Weslaco, Texas during Jan, Feb, and Mar 1965, at Key West and Bradenton, Florida, and at 7 areas in Puerto Rico.

Two important meetings with great potentialities for coordination of the *Aedes aegypti* eradication activities of this Branch with those of other agencies were held during the first quarter of 1965.

Entomologists of the Department of Defense met with personnel of the Aedes aegypti Eradication Branch in Atlanta on Feb 24–25, 1965, to discuss the coordination of survey and eradication measures for *Aedes aegypti* on military reservations with those of the Cooperative CDC-State Health Department Programs in civilian areas. There were 48 people at this 2-day conference including 14 from the Army, 7 from the Navy, and 14 from the Air Force. Since that time training courses have been held with Army and Air Force personnel and inspections are being made on military reservations by Army and Air Force personnel in the United States and Puerto Rico.

A conference sponsored jointly by the American Medical Association and the Communicable Disease Center was held in Atlanta, Mar 4–5, 1965, to discuss cooperative activities involved in carrying out the *Aedes aegypti* eradication program. The Aedes aegypti Eradication Branch of CDC is working clocolosely with AMA in stimulating interest in the program and support for it from both private physicians and the general public. Some 75 delegates to the conference, representing health departments and medical societies in areas with *Aedes aegypti* infestations, heard panel discussions on, "The Impact of the *Aedes aegypti* Eradication Program on State and Local Health Departments", "The Role of Private Physicians in *Aedes aegypti* Eradication," and "Achieving Professional and Public Support".

A new color sound motion picture "Enemy In Your Home" was completed and shown for the first time at this AMA meeting. Copies of this film have been purchased and are available on short term loan from the CDC Film Library, the Aedes aegypti Eradication Branch at CDC in Atlanta, Ga., or the

various Area Offices in Florida, Texas, Puerto Rico, and the Virgin Islands.

In early June 1965 Research Field Investigations were initiated in Perrine, Florida. Extensive research is underway to evaluate equipment for dispensing DDT and the extensiveness of application necessary to achieve eradication, to develop procedures for insecticidal treatment of water-holding plants, to determine the effectiveness of insecticidal treatment in dry containers, and to conduct studies on the effects of operational spraying with DDT on wildlife in the area. This last study is being conducted in cooperation with the Fish and Wildlife Service which has established protocol for this study.

KNOW YOUR WORLD

Did You Know?

That an outbreak of dengue began in the State of Yaracuy, Venezuela in late August 1965, with 837 cases being reported up to 2 October 1965?

Seventeen other states with 2,504 cases have been affected so far in 1965. However, no cases have been reported from Antigua, Jamaica or Puerto Rico since 3 July, 4 September and 14 August 1965, respectively. The totals for those islands in 1965 are: 8, 31, and 89 cases. Dengue has not been reported so far this year in other areas of the Caribbean region. (1)

That emphysema, a chronic respiratory disease, is second among all disabilities for which workers are awarded Social Security Benefits? (2)

That in the Ruhr Basin of West Germany, where air is heavily polluted, over 15% of the children were reported to show symptoms of rickets in 1961? (3)

That an outbreak of 64 cases of louse-borne typhus, with 5 deaths, has occurred in 5 localities of Angaraes Province, Huancavelica Department, Peru, from December 1964 to September 1965?

This outbreak was characterized by the occurrence of mild clinical forms and with a low fatality rate. The disease is not known to previously occur in these localities. (4)

That a military dependent of an American serviceman, residing in the Mediterranean area was admitted to a station hospital because she was passing worms?

A total of 25 "worms" were passed and 3 were sent to a laboratory for identification. They proved to be 4th instar fly larvae. One larva was still alive, and the medical entomologist was able to rear it to the adult stage, which was tentatively identified as *Sarcophaga haemorrhiodalis*, the Red-tailed Flesh Fly. It was later found that the patient had eaten a plate of raw clams about a week before passing the maggots.

James, M. T., 1947, p 49, states that the above species is almost worldwide in distribution, and describes cases similar to the above. Ulcers have been caused in the intestinal wall, and he concludes that the parasite seems capable of causing considerable injury. The larvae of flies in this genus are usually alive, and are said to soon disappear into the food medium. This would explain why raw clams could be eaten without realizing that they contained fly maggots. (5)

That the malaria-carrying mosquito *Aedes aegypti* has returned to El Salvador, apparently by means of a shipment of imported used tires?

The mosquito was found recently in San Salvador; foci of reinfestation were discovered subsequently in the city. Breeding larvae were found in tires in 6 of the 14 infested premises. Tires collecting rainwater furnish an ideal breeding place of the *A. aegypti*. The Pan American Sanitary Bureau reports that *A. aegypti* was eradicated in El Salvador in 1957, and periodic inspections for reinfestation have been negative until now. (6)

That the Fifth Asian Malaria Conference was held in Colombo, Ceylon from 20–27 October 1965 under the sponsorship of the WHO?

Twenty-one countries or territories were represented by their national health services and chief malariologists: Afghanistan; Australia; British Solomon Islands; Brunei; Cambodia; Ceylon; China (Taiwan); India; Indonesia; Japan; Korea; Laos; Malaysia; Maldive Islands; Nepal; Pakistan; Philippines; Ryukyus Islands; Thailand; Timor Dili and Viet Nam. Together, they represent 80% of the global malaria eradication campaign launched 10 years ago by WHO. (7)

That two babies in Saratoga County are the first Upstate cases of phenylketonuria (PKU) detected under the State of New York mandatory testing law?

Two other PKU infants were found in New York City in February 1965. The law, effected on 1 January 1965, requires that every baby born in the State must be tested for the hereditary disease. Treatment consists of a special diet low in foods containing phenylalanine (assimilate phenylalanine, a common food substance found in protein foods). PKU testing costs about $224,000 a year to the State. Preventing mental retardation in just one case of PKU infant saves $150,000 for life of infant. The new law makes both the person who registers the birth (usually the attending physician) and the administrator of the hospital where the baby was born responsible for testing. (8)

That dollar-wise the pet foods industry is 2½ times as big as the baby foods industry? (9)

That it is estimated that 198,000 arthritics are less than 25 years of age?

Arthritis disables more people than any other chronic disease, except heart disease, this being true for both sexes, white and nonwhite persons, and in all family income categories. (10)

That a new pulp and paper mill has been built by a Wisconsin-based company on the Sacramento river in California without mill wastes fouling the river?

The company and the state, working together, demonstrated that clean streams and recreational opportunities can exist together with industrial development. Ten percent of the $20 million plant cost was spent on pollution control facilities. Efficiency of the waste control program is found in the fact that salmon continue to spawn downstream from the plant which puts 10 million gallons of treated effluent into the river daily. Wisconsin, one of few states, encourages development of such waste control facilities through state tax relief, while federal tax relief is contemplated. (11)

That the Maldive Islands has become the 122nd full Member of the World Health Organization (WHO) in November 1965?

The Maldive Islands are situated to the southwest of India and Ceylon; consisting of some 20 atolls totalling about 2,000 islands of which about 200 are inhabited. Fishing industry accounts for over 90% of the total revenue. (12)

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EDITORIAL DESK

AMERICAN BOARD OF OB-GYN
(PART I EXAMINATION)

The next Part I (written) examination of this Board will be given at 10:00 a.m. on Saturday, July 2, 1966 at designated examining centers in the United States, Canada, and military bases outside of the continental United States.

Physicians who will have completed an approved progressive residency training program, including eighteen months each of obstetrics and gynecology, as of June 30, 1966 will be eligible to apply during January or February for this examination.

Application forms and current Bulletins may be obtained by writing to the office of the Secretary, Clyde L. Randall MD, American Board of Obstetrics and Gynecology, Inc., 100 Meadow Road, Buffalo, New York, 14216.

Diplomates of this Board are continually urged to notify the Secretary's office of a change in address.

MEMBER OF AMERICAN OCCUPATIONAL THERAPY PLANNING GROUP

CDR Barbara Munroe MSC USN, Chief of the Physical Medicine Training Division, U.S. Naval Medical School, National Naval Medical Center, Bethesda, Maryland, represented the Bureau of Medicine and Surgery at the pre-conference meetings of the American Occupational Therapy Association at the Hotel Americana, Miami Beach, Florida, 29–31 October 1965. Participants in the pre-conference meetings were members of the various committees of

the American Occupational Therapy Association. The group met prior to the 45th Annual Conference in order to formulate plans for the improvement of the academic and clinical education of occupational therapists.

CDR Munroe was also a participant in the workshop entitled "Role and Function of the Certified Occupational Therapy Assistant in Relation to the Registered Occupational Therapist" which was held from 30 September to 2 October 1965 in Chicago, Illinois. The workshop was sponsored by the American Occupational Therapy Association.—CO, NNMS, Bethesda, Md.

FIRST SUBMARINE MEDICAL OFFICERS TO QUALIFY UNDER NEW RULES

Lieutenants W. L. Dennison Jr. and J. H. Earls, Medical Corps, United States Navy, achieved distinction on October 29, when they became the first physicians to receive the designation of Qualified Submarine Medical officers under the new rules established by the Bureau of Naval Personnel, which delegated sole authority for qualification of submarine medical officers to the Commanding Officer, U.S. Naval Submarine Medical Center.

Submariners "dolphins", the hard earned insignia of the Navy's underwater fleet were pinned on the physicians by their Commanding Officer, CAPT C. L. Waite MC, Commanding Officer of the Medical Center, Submarine Base New London, Groton, Connecticut.

Doctor Dennison is from Princeton, N. J. and a graduate of Jefferson Medical College in Philadelphia, Penn. After completion of the Course in Submarine Medicine he was assigned to the Gold Crew of the USS ABRAHAM LINCOLN (SSBN-602). Doctor Earls' home is in Shawnee, Oklahoma and he received his M.D. degree from Oklahoma University Medical School. Following completion of the Course in Submarine Medicine he was assigned to the Blue Crew of the USS ETHAN ALLEN (SSBN-608). Both physicians are instructors at the School of Submarine Medicine, a department of the Medical Center.

Submarine medicine became a recognized military medical specialty during World War II. In 1943, the Bureau of Naval Personnel established the qualification requirements, the insignia or the "medical dolphins," and began qualifying submarine medical officers, until the present time. Prior to the war there were no more than ten medical officers actively engaged in the practice of submarine medicine. The greatest number of qualified submarine medical officers existing at any one time during the course of the war was twenty-seven. The rapid growth of the submarine medicine program has been due to the construction of the Navy's Polaris submarines. Each of these submarines has two complete crews known as Blue and Gold. A medical officer is assigned to each crew. During calendar year 1964, the School of Submarine Medicine graduated 68 medical officers and at the present time there are approximately 120 submarine and diving billets.

To achieve qualification, medical officers must be graduates of the 23-week Course in Submarine Medicine, serve a minimum of three months probation in a submarine or diving billet, publish a thesis pertaining to submarine or diving medicine, satisfactorily complete a comprehensive examination and be recommended by their commanding officers.—Public Information Officer, U.S. Naval Submarine Base New London, Groton, Conn. . . . Applications for the class in Submarine and Diving Medicine for the class convening in July 1966 are still being accepted. For further information regarding this program, address inquiries to: Director, Submarine and Radiation Medicine Division, Bureau of Medicine and Surgery, Department of the Navy, Washington, D.C. 20390.

FEDERAL NURSING PROGRAM OF THE ASSOCIATION OF MILITARY SURGEONS' ANNUAL MEETING

CAPT Ruth A. Erickson NC USN, Director, Navy Nurse Corps, presided at the Nursing Section Program of the 72nd annual meeting of the Association of Military Surgeons on Tuesday, 16 November 1965. Doctor Eleanor C. Lambertsen, Director, Division of Nursing Education, Teachers College, Columbia University and Colonel Kenneth D. Orr MC USA, Commanding Officer, Valley Forge General Hospital, presented a panel discussion on "Programming for Patient Care." The program attracted a capacity audience with nurse representation from the military, federal services and civilian institutions.—Nursing Division, BuMed.

AMA CONTINUES APPROVAL OF NAVMEDSCOL X-RAY COURSE

The Council on Medical Education of the American Medical Association recently revised their requirements for the training and accreditation of X-ray Technicians. The new requirements include:

1. The extension of the training period by one full year for a total course length of two years.

2. An increase in the didactic phase of the instruction to a minimum of 420 hours.

To meet these requirements established by the AMA, the U.S. Naval Medical School course for the training of X-ray Technicians was revised, and the required two-year program was arranged. The first year is divided into two phases. During the first twenty-six weeks the trainees receive a total of 453 didactic hours. The didactic phase, which is 33 hours in excess of the minimum requirement of the AMA, is taught at the U.S. Naval Medical School in Bethesda, Maryland. This is the only Military X-ray Course currently approved by the AMA. Students who successfully complete this phase of the program are then transferred to Naval Hospitals for an additional twenty-six week period of on-the-job training. In the second year of the program, each technician must serve under the supervision of a qualified Board Radiologist in order to establish eligibility for registration with the National X-Ray Societies.

Recently an inspection team from the American Medical Association visited the X-ray Division of the U.S. Naval Medical School, NNMC, Bethesda, Maryland. It reviewed the facilities, course materials, instructor and student personnel, as well as course content of the new program. Their findings and recommendations were forwarded to the AMA for approval.

Recently, the decision of the AMA was relayed to the U.S. Naval Medical School, and the letter reads in part as follows:

"The Council on Medical Education of the American Medical Association at its meeting on June 18, 1965, concurred with the Committee on Technician Training of the American College of Radiology, that approval of the School of X-ray Technology be continued.

"We extend best wishes for continuing success in the operation of the training program."

U.S. NAVAL MEDICAL SCHOOL EXPANDS PROGRAM FOR THE CONTINUING EDUCATION OF MEDICAL OFFICERS

The current military situation demands rapid dissemination of the most recent scientific information among medical officers in all branches of the services. To meet this demand, CAPT John H. Stover Jr. MC USN, Commanding Officer of the U.S. Naval Medical School has announced the initiation of two different types of interlocking programs. Traveling teaching teams, composed of groups of specialists prepared to present courses dealing with medical problems of military interest, have been organized. In addition, a library of instructional films is being developed for circulation among various military hospitals.

The first briefing team traveled to the U.S. Naval School of Aviation Medicine, U.S. Naval Aviation Medical Center, Pensacola, Florida to present a one-week course in "Nuclear, Biological and Chemical Warfare Defense" beginning 18 October 1965. The team included staff members from the U.S. Naval Medical School augmented by personnel from the Nuclear Weapons Training Center, Atlantic, Norfolk, Virginia. A unique set of visual aids and other teaching materials had been assembled and prepared to support this program. The course consisted of a series of lectures and demonstrations which emphasize the medical aspects of special weapons and delineate the medical department responsibilities in defense against their possible use by an enemy.

A library of informative films is being developed and assembled at the U.S. Naval Medical School. The 16 mm. sound films are being produced through the cooperative efforts of the Naval Photographic Center, Washington, D.C., and the Graphic Arts Department of the U.S. Naval Medical School. These films contain the most recent information on topics of current military interest. Several kinescope recordings dealing with particular aspects of tropical diseases and field medicine have been completed. Recordings of lectures concerned with the medical implications of modern weapons systems are also in production.

Plans have been formulated for the expansion of the series to embrace other aspects of medicine. Included will be topics of general medical interest, e.g. Nuclear Medicine, a clinical and pathological series, as well as subjects of more specific military interest such as the "Role of Medicine in Counter-Insurgency." The great number of professional lectures and conferences conducted annually at the National Naval Medical Center is a rich source of information on medical matters. The technique of video-tape to 16 mm. sound film transfer makes it possible to record and prepare for circulation these outstanding lectures for distribution to other Naval medical activities to supplement their professional educational programs.

Detailed information regarding the nature and availability of the teaching teams as well as the titles

of specific informational films that are available may be obtained by writing to:

Commanding Officer
U.S. Naval Medical School
National Naval Medical Center
Bethesda, Maryland 20014

PRESENTATION OF LEGION OF MERIT

The President of the United States takes pleasure in presenting the Legion of Merit to CAPT Walter F. Mazzone MSC USNR for service as set forth in the following citation:

"For exceptionally meritorious service from 1 September 1963 to 4 August 1964 as Medical Technical Officer for Project SEALAB I. Working tirelessly and effectively to insure the success of the United States Navy's first undersea dwelling in which the inhabitants lived for a period of eleven days at a depth of 192 feet in the open ocean under ambient conditions, CAPT Mazzone brilliantly supervised the preparation and fitting out of the SEALAB dwelling and prepared the mixed gas tables used to form the structure's atmosphere. Additionally, he designed and operated the equipment which provided this breathing medium to the SEALAB inhabitants and, by making numerous dives from the surface, insured the safety of the inhabitants and diving photographers. He further supervised the physiological tests, the results of which have materially enriched the field of underwater research and greatly assisted the United States Navy's deep submergence effort towards its ultimate goals. CAPT Mazzone's leadership, professional competence, and devotion to duty were in keeping with the highest traditions of the United States Naval Service."

CAREFUL CORPSMAN

This small Vietnamese boy exhibits trust in the treatment administered by Hospital Corpsman Second Class B. J. Bein, USN. The corpsman is a member of a medical aid team, attached to the 3rd Tank Battalion, Third Marine Division, treating civilians in two hamlets near Da Nang Airfield, Republic of Vietnam.—Armed Forces Press File.

17 MAJOR ADVANCES IN DRUG THERAPY

1. *Chlorothiazide*—this first oral thiazide diuretic for the treatment of high blood pressure and water retention by the body, was called ". . . among the most useful—and widely used—of therapeutic agents."

2. Spironolactone—an aldosterone-antagonist diuretic used alone or with other diuretics.

3. *Imipramine*—selected as effective in many patients with severe depressions. Amitriptyline, introduced in 1965, also was highly regarded.

4. *Griseofulvin*—an oral drug effective in the treatment of many common fungous infections of the skin and nails resistant to drugs applied directly to the skin.

5. *Amphotericin B*—the first reliable weapon against serious systemic fungous infections.

6. The *semi-synthetic penicillins*—a number of which were said to be effective against staphylococcal organisms resistant to ordinary penicillin.

7. *Anticancer drugs*—though none cures cancer, all the 15 drugs for the treatment of leukemia and of solid tumors discussed by The Medical Letter during its first six years, when used singly and in various combinations, have proved effective in some patients in bringing about remissions, lasting from a few months to several years. The anticancer agents considered most valuable are: 5-fluorouracil, cyclophosphamide, vinblastine sulfate, triethylenethiophosphoramide and dactinomycin.

8. *Triamcinolone acetonide*—this steroid preparation applied to the skin, has proved to be more effective against many skin disorders than comparable preparation previously available.

9. *Phenformin*—the panel agreed that this new oral drug has "unique usefulness" in enabling many diabetic patients to control blood sugar levels without daily insulin injections; although the oldest of the oral antidiabetic agents, tolbutamide remains the most widely used.

10. *Nalorphine*—a narcotic antagonist which combats both withdrawal symptoms in drug addicts and the respiratory depression caused by excessive doses of narcotic drugs. The poll turned up little

enthusiasm for any of the new analgesics and narcotics introduced in recent years.

11. and 12. *Sabin live-virus polio vaccine and the measles vaccines*—were almost unanimously selected as major contributions to preventive medicine.

13. *Halothane*—a non-explosive anesthetic agent that has virtually replaced ether in the operating room.

14. and 15. *Oral contraceptives and intrauterine contraceptive devices*—both were regarded by a majority of the consultants as major medical advances.

16. *D-penicillinamine*—an oral chelating agent was chosen as the most effective drug yet available for the treatment of Wilson's disease, a rare disorder in which large excesses of copper are deposited in various parts of the body.

17. *Glucagon*—a drug for the emergency treatment of insulin shock when the patient cannot take sugar orally.

In the copies of The Medical Letter contained in the new volume, more than two-thirds of the drugs reviewed were considered to have no proven advantage over previously available remedies, a small percentage was found to be excessively hazardous.

The Medical Letter's editorial board, under whose direction the volume was prepared, consists of Harold Aaron, M.D., New York internist; Lytt I. Gardner, M.D., professor of pediatrics, State University of New York, Upstate Medical Center; and Jules Hirsch, M.D., associate professor, Rockefeller University.

The publication's advisory board, whose members also review all drug appraisals, includes: Louis S. Goodman, M.D., professor and head of the Department of Pharmacology, University of Utah College of Medicine; Louis C. Lasagna, M.D., associate professor of medicine and director of the Division of Clinical Pharmacology at Johns Hopkins Medical School; Paul H. Lavietes, M.D., associate clinical professor of medicine, Yale University Medical School; Mark H. Lepper, M.D., professor and chairman of the Department of Preventive Medicine, University of Illinois Medical School; George E. Moore, M.D., clinical professor of surgery, State University of N.Y. at Buffalo, and director, Roswell Park Memorial Institute; Maxwell M. Wintrobe, M.D., professor and head of the Department of Medicine, University of Utah College of Medicine; Robert I. Wise, M.D., professor and head of the Department of Medicine, Jefferson Medical College. —The Medical Letter.

ADVANCED COURSE IN NUCLEAR SCIENCE FOR MEDICAL OFFICERS (NSMO)

Sponsored by the Defense Atomic Support Agency (DASA) at the University of Rochester, Rochester, New York.

CLASS	INCLUSIVE DATES
#19	27 June 1966 - July 1967

DEADLINE DATE TO APPLY	SECURITY CLEARANCE REQUIREMENTS
1 March 1966	TOP SECRET

Mission: It is the mission of the NSMO Course to provide the opportunity for a limited number of selected Army, Navy and Air Force Medical Officers to acquire the additional technical education needed to cope with the radiobiological problems involved in all phases of the National nuclear energy program.

Scope: The course provides for a review of selected portions of mathematics and physics during the refresher phase, followed by a full academic year of graduate study involving radiological physics, health physics, biological effects of radiation, evaluation of radiation hazards, environmental hygiene and toxicology, and as electives, related areas of industrial medicine and radiology. Completion of the academic phase at acceptable performance levels can lead to a Master's Degree in Radiation Biology, in one year for those entering with doctoral degree and upon completion of additional research or special studies for those not having previous professional training. The academic phase is followed by a study of practical military nuclear medicine. During the course the medical aspects of nuclear radiation over the complete range of intensity levels from low-level, peace-time laboratory situations through high-level, full scale nuclear warfare situations are discussed.

PHASE I (9 weeks). Academic Refresher—Summer School Session, University of Rochester, Rochester, New York.

PHASE II (10 months). Radiation Biology—School of Medicine and Dentistry, University of Rochester, Rochester, New York.

PHASE III (4 weeks). Military Nuclear Medicine —National Atomic Weapons Capabilities, Course (NAC) (9 academic days), Field Command, DASA, Sandia Base, Albuquerque, New Mexico. Remainder to be announced.

Eligibility: The course is primarily designed for

officers of the Medical Corps. However, officers of the Medical Service Corps, in very closely allied medical fields who have had some graduate work beyond the B.S. degree may also be eligible for selection.

Requests should be forwarded in accordance with BUMED INSTRUCTION 1520.10C and comply with the deadline date as indicated above. All requests must indicate that a security clearance of TOP SECRET has been granted to the officer requesting attendance, or that action to obtain clearance has been initiated.—Training Branch, BuMed.

IMPORTANT NOTICE

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—Editor

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